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EDEMA IN PRE-ECLAMPSIA AND ECLAMPSIA*

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THE slight pitting edema of the ankles found in most pregnant patients late in pregnancy may be attributed to the increased venous pressure, as demonstrated by Burwell. Pitting edema over the tibiae is an abnormal occurrence in the absence of varicosities or a previous phlebitis. Edema of the face, hands, abdominal wall, vulva, or body cavities is always an abnormal finding. We have observed that 35 per cent of all types of toxemic patients had no demonstrable pitting edema of the pretibial tissues, and an additional 34 per cent had only slight edema of these tissues.

Studies of the physiology of normal pregnant and toxemic women have been made by us over the past sixteen years. Over 2,700 patients with toxemia have been observed by us, and various examinations have been made in the majority of cases. We believe that our data, as well as those reported in the literature, indicate that the changes incidental to normal pregnancy, namely, an increased capillary permeability and a delayed or impaired water and sodium chloride elimination, are greatly augmented in certain patients, due either to internal or external factors, resulting in an abnormal gain in weight and, eventually, in edema.

Excess salts, water or products of metabolism are eliminated from the circulation by way of the kidneys. If the renal excretion is slow they pass into the tissue spaces, remaining there until they can be excreted. An abnormal amount of water or sodium chloride, either ingested or

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injected parenterally, may thus initiate an edematous or pre-edematous condition. The occurrence of edema should be regarded as a chain of events in which an initial abnormality causes a series of subsequent changes. The various factors in the chain are fairly well recognized, but the primary abnormality and the consequences are still moot points for discussion.

The various primary and secondary factors which may be concerned in the formation of edema in pre-eclampsia and eclampsia are as follows:

1. A decreased colloid osmotic or oncotic pressure of the serum proteins.
2. An increased permeability of the capillary walls.
3. An increased capillary pressure.

Contributory factors, which are of importance, are:

1. A decreased tissue pressure.
2. An increased concentration of proteins in the tissue fluids.
3. A warm environment.
4. An impaired elimination of water or of sodium chloride, or an excessive ingestion of either, or both.
5. An abnormal hormone metabolism.

Edema is likely to occur if the colloid osmotic pressure of the serum proteins is less than 20 cm. of water. Such a low pressure is usually associated with a serum protein concentration of less than 5.5 ± 0.3 Gm. per cent, or a serum albumin concentration of less than 2.5 ± 0.2 Gm. per cent. The average serum protein concentration for normal individuals, based on reports in the literature, is 7.5 ± 0.51 Gm. per cent, with a range of from 6 to 8.3 per cent. A number of observations have been made on the concentration of the plasma or serum protein in pregnant patients. The figures for plasma protein include fibrinogen, which exerts little, if any, osmotic pressure, but amounts to 0.43 Gm. per cent in plasma from pregnant patients. We have, therefore, always determined the concentration of the serum proteins. The average serum protein concentration in normal pregnant patients, calculated from 17 reports, is 6.5 Gm. per cent; the minimum average figure is 5.75, and the maximum is 7.9 Gm. per cent. The average was less than 6.2 Gm. per cent in only two reports.

The figures for serum albumin are not as numerous and range from 2.96 to 4.07, with an average of 3.72 Gm. per cent. The serum globulin range is from 2.2 to 3.83, with an average of 2.90 Gm. per cent. The albumin:globulin ratio ranges from 0.97 to 1.8, with an average of 1.33. Our average serum albumin is 3.66, globulin 3.00 Gm. per cent, and the albumin:globulin ratio is 1.22. In toxemic patients with edema the serum albumin is 3.24 Gm. per cent, and the albumin:globulin ratio is 1.04.

The reported averages for serum protein and albumin concentrations in toxemic patients are listed in Table I. We have calculated the colloid osmotic pressures, with the exception of Strauss' data. The concentrations of both serum protein and albumin are decreased, but with the exception of two, are above the edema level. Strauss' calculated oncotic pressure for eclampsia is less than 20 cm. Harden's data are interesting

TABLE I. REPORTED DATA FOR SERUM PROTEIN FRACTIONS AND COLLOID OSMOTIC PRESSURE IN TOXEMIC PATIENTS

AUTHOR	DIAGNOSIS	SERUM		COLLOID OSMOTIC PRESSURE CALCULATED* CM. WATER
		PROTEIN GM.	ALBUMIN %	
Eastman	Pre-eclampsia	5.4	3.1	22.0
	Eclampsia	6.3	3.5	27.0
	Low-reserve kidney	6.2	3.8	27.0
Plass and Bogert	Pre-eclampsia	5.17		
	Eclampsia	5.77		
Strauss	Pre-eclampsia	5.5	3.1	21.5
	Eclampsia	4.9	2.6	17.5
Harden	1. Pre-eclampsia	6.58	3.81	29.0
	2. Pre-eclampsia	5.60	3.42	23.0
	1. Eclampsia	6.37	3.82	28.0
	2. Eclampsia	4.97	3.16	24.0
Bergman	Edema, slight	6.44		
	Edema, marked	6.04		

*Wells' formula: 1, No protein stabilization; 2, with protein stabilization.

because he stated that if enough protein is ingested to equal the metabolic needs and the protein lost in the urine, the patient improves clinically and the incidence of eclampsia is markedly reduced. His figures for serum protein and albumin concentrations were slightly less in patients who were in "protein stabilization" than in those obtained on admission.

The average colloid pressure in the various reports listed by Drinker and Fields is 35.7, with a range of 26.4 to 46.5 cm. of water, for normal individuals. Only a few figures are available for the determined oncotic pressure in pregnant patients. Runge and Kessler report that it is 36.4 cm. in early pregnancy, and 27.6 at term. Kaboth's figure is 31.5 cm. of water at term.

We have determined the serum protein and albumin concentrations and the colloid osmotic pressure, using Wells' method for the latter determination, in a number of normal pregnant and toxemic patients before and after delivery. Our data are summarized in Table II. We have found that the colloid osmotic pressure is 28.7 cm. in normal pregnant patients at term, 24.9 cm. in toxemic patients with edema, and 26.5 cm. in those without edema. The average calculated pressure for toxemic patients, based on published reports, is 24.9 cm. Oncotic pressures and serum protein determinations were made on the same patients after delivery. These data serve as controls, since the post-partum pressures for normal patients are all within the normal range. Many factors are concerned in the formation and disappearance of edema, but the consensus of opinion is that edema is likely to occur if the oncotic pressure is less than 20 cm., and likely to disappear if the pressure exceeds this figure. The majority of our pressures are above this figure. Furthermore, the determined and calculated osmotic pressures coincide. Therefore, there are no intrinsic changes in the serum proteins, which might account for the edema, as we have postulated several years ago.

TABLE II. SERUM PROTEIN AND ALBUMIN CONCENTRATIONS AND COLLOID OSMOTIC PRESSURE IN PREGNANT PATIENTS

	NORMAL PREGNANCY		TOXEMIC PREGNANCY			
			WITH EDEMA		WITHOUT EDEMA	
	NO. OF PATIENTS	MEAN	NO. OF PATIENTS	MEAN	NO. OF PATIENTS	MEAN
Serum Protein, Gm. %						
Ante partum	15	6.66 ± 0.06	14	6.34 ± 0.12	8	6.38
Post partum	12	7.12 ± 0.05	14	7.12 ± 0.13		
Serum Albumin, Gm. %						
Ante partum	15	3.66 ± 0.06	14	3.24 ± 0.09	8	3.3
Post partum	12	3.81 ± 0.07	14	3.32 ± 0.09		
Determined Colloid Osmotic Pressure, cm. water						
Ante partum	15	28.7 ± 0.64	14	24.9 ± 0.78	8	26.5
Post partum	12	32.9 ± 0.56	14	28.6 ± 0.67		
Calculated Colloid Osmotic Pressure, Wells' formula, cm. water						
Ante partum	15	28.9 ± 0.52	14	25.9 ± 0.70	8	27.5
Post partum	12	32.0 ± 0.47	14	29.1 ± 0.56		

TABLE III. SERUM PROTEIN CONCENTRATION IN DIFFERENT GROUPS OF TOXEMIC PATIENTS

TYPE OF TOXEMIA	NO. OF PATIENTS	YEAR	SERUM PROTEIN	
			MEAN GM. %	RANGE GM. %
Pre-eclampsia, all patients	36	1933	5.92 ± 0.08	4.0 – 7.4
Pre-eclampsia, all patients	41	1938	6.43 ± 0.08	4.6 – 7.5
Pre-eclampsia, edematous	116	1940	6.22 ± 0.04	4.5 – 7.4
Pre-eclampsia, edema 1 +	12	1940	6.55 ± 0.08	6.0 – 7.4
Pre-eclampsia, edema 4 +	30	1940	6.22 ± 0.06	4.6 – 7.4
Eclampsia, all patients	41	1936	6.70 ± 0.07	5.1 – 8.4
Eclampsia, edema 1 +	19	1940	6.36 ± 0.12	5.0 – 7.9
Eclampsia, edema 4 +	65	1940	6.37 ± 0.07	4.5 – 8.5
Vascular-renal, all patients	57	1933	6.36 ± 0.05	5.0 – 8.4
Vascular-renal, all patients	62	1938	6.71 ± 0.05	5.1 – 8.3
Vascular-renal, edematous	87	1940	6.67 ± 0.04	5.2 – 7.9
Vascular-renal, edema 4 +	41	1940	6.09 ± 0.06	4.6 – 7.6

We have made serum protein determinations on the various groups of toxemic patients listed in Table III. The patients in the 1940 group had varying amounts of pitting edema, and an additional evidence of excessive water retention was that all of them lost at least 12 or more kilograms in weight in the post-partum period. If there was more than one determination of serum protein before delivery, the lowest figure was used. We have omitted all patients with acute or chronic glomerulonephritis, or with marked renal impairment from nephrosclerosis. The post-partum figures for the urea clearance were 74 per cent after pre-eclampsia, 80 per cent after eclampsia, and 70 per cent for the vascular-renal disease group, indicating normal renal function. A further division of patients having a 1+ edema, and those with a 4+ edema, was made, but it showed no correlation between the serum protein concentration and the amount of edema. The means for pre-eclampsia and

eclampsia were 6.22 and 6.36 Gm. per cent, respectively. These figures, as well as the fact that only 16 per cent of the pre-eclamptic, and 12 per cent of the eclamptic patients had a serum protein concentration of 5.5 Gm. or less, indicate that the cause of the edema in over 80 per cent of our toxemic patients is not due to a hypoproteinemia.

TABLE IV. PERCENTAGE OF PATIENTS WITH SERUM PROTEIN CONCENTRATION OF LESS THAN

	GRAMS PER CENT		
	5.0	5.6	6.0
Pre-eclampsia	4	16	39
Eclampsia, edema 1 +	0	11	37
Eclampsia, edema 4 +	5	12	37
Vascular-renal disease, edematous	0	6	18

The average serum protein concentration at two weeks post partum for the same patients was 6.85 ± 0.05 for those with pre-eclampsia; 6.85 ± 0.06 for those with eclampsia, and 7.1 ± 0.04 for those in the vascular-renal group.

We have believed for many years that the edema was not due to a hypoproteinemia, and we have repeatedly stated that a marked blood dilution occurred preceding clinical improvement, associated with an average *decrease* of 14 per cent in the serum protein concentration in pre-eclampsia, and 25 per cent in eclampsia; and that the diuresis, disappearance of the edema, negative sodium chloride and water balance, and greatest weight loss occurred when the serum protein concentration was lowest.

An increased permeability of the capillary wall has been suggested as the cause of certain types of edema. The capillary wall may be injured by prolonged anoxemia or by certain poisons; for example, those apparently associated with acute glomerulonephritis and epidemic dropsy. Some toxin or hormone which alters the capillary wall may be the primary cause of the edema found in pre-eclamptic patients. Unfortunately, there are no measurements for directly determining the capillary permeability.

Petersen and Lash have attempted to detect changes in the capillary permeability by an indirect method. They have determined the protein content of blister fluid and have noted that the amount of protein is increased in pregnant and edematous patients. Our results varied, but, generally, were confirmatory in a small series of patients. Unfortunately, this method is painful.

Lash, using the intradermal salt solution test, found that the wheal disappeared more rapidly in pregnant than in nonpregnant patients, and that the time of disappearance was shorter on the leg than on the forearm. In the toxemias of pregnancy, the disappearance time became extremely short and was due presumably to the high protein content of the subcutaneous fluids. The test is simple and striking, but all types of edema in pregnancy gave similar results.

Landis states that the average arteriolar capillary pressure is 45 cm. of water, and the venous capillary pressure is about 22 cm. Reported observations in pregnant patients are at variance. We believe that all the data at hand indicate that in both normal and pregnant toxemic patients the arterial capillary pressure is within the normal range.

The venous capillary pressure is dependent largely on the venous pressure. If the latter becomes too high, the capillary pressure will exceed the oncotic pressure of the serum proteins and fluid will not be absorbed from the tissues. Thomson, Reid, and Cohen reported no change in the arm venous pressure in pregnant women. They found, however, in a small group of toxemic patients, that more values fell within the upper normal range.

Burwell has reported that the average venous pressure in pregnant patients at term is 9.0 for the arm, and 20 cm. for the leg. He found the average venous pressure in nonpregnant individuals to be 5.8 cm. for both the arm and the leg. He observed that this difference in pressure began at the fourth month of pregnancy and slowly increased throughout pregnancy, but that after delivery the leg venous pressure fell rapidly to normal. He studied these pressures in pregnant bitches and found comparable changes to those observed in pregnant women. He noted that if the intra-abdominal pressure became increased by the injection of salt solution, the leg pressure also increased. He did not ascribe much importance to this observation in the human individual because the abdominal wall is never as tense as it is in the experimental animal. If the gravid uterus was supported so that it did not press on the pelvic veins, the pressure in the femoral veins decreased, although it still remained above that in the jugular veins. He attributed this remaining increased pressure to the effect of the placental circulation, which resembles an arteriovenous fistula.

Landis and his co-workers have demonstrated that fluid accumulates in the tissue spaces when the venous pressure is greater than 15 to 20 cm. of water. Increased temperatures also resulted in a greater filtration rate, which accounts for the increased incidence of edema in pregnant patients in hot weather.

Thompson, Thompson, and Dailey have demonstrated that when the human subject stands quietly the blood volume is diminished by as much as 400 c.c., as fluid filters from the blood into the tissues of the legs. This fluid contains relatively little protein, so that the protein percentage of the circulating blood rises while the subject stands still. This phenomenon may explain some of the discrepancies in reported observations of serum protein concentrations in various conditions.

Youmans and co-workers have studied the serum protein concentration, colloid osmotic pressure, and leg volume in normal individuals. They found that standing at an angle of 75 degrees for approximately one hour caused an increase of from 18 to 40 per cent in the concentration of the serum protein, and an increase of from 29 to 65 per cent in the colloid osmotic pressure of the blood in the foot of normal subjects. The increase in the concentration of protein and in the osmotic pressure was approximately twice as great as that which occurred in the blood from the arm. The volume of the leg increased from 3.11 to 4.87 c.c. per 100 c.c. of leg, but pitting edema did not occur in any of the normal subjects. Patients with nutritional edema showed essentially similar changes, with a demonstrable increase in pitting edema. Calculations based on the data obtained suggest that the increase in the tissue pressure was from three to five times as important in limiting the loss of fluid from the blood, as was the increase in the colloid osmotic pressure.

We have obtained blood from an arm vein in a small number of edematous pregnant patients at rest in bed, and then blood from the arm and foot after the patient had had her legs hanging out of bed for ninety minutes. The difference in the arm cell volume and the serum protein concentration may amount to as much as 19 and 23 per cent, respectively; and the difference between the resting arm blood and the hanging leg blood may amount to as much as 9 per cent for the hematocrit, and 21 per cent for the serum protein. This method of determining the rate of filtration in the legs caused by an increased venous pressure may be of value in detecting potential pre-eclamptic patients.

Keys and Taylor have demonstrated that during severe work the blood becomes concentrated, due to the movement of the filtrate, which is low in protein, from

the blood into the tissues. They found that although the serum protein concentration increased, the colloid osmotic pressure definitely decreased. They concluded that the filtrable protein must be approximately at least five times as active osmotically as nonfiltrable protein. Their observations, as well as the preceding ones, indicate the value of bed rest in the treatment of edema and toxemia.

Burch and Sodeman state that the average tissue pressure in normal subjects amounts to 17.9 mm. of water. Using their method, Brown and myself, in a small series of patients, have found that the tissue pressure is increased slightly in normal pregnant patients, and markedly in those with edema. An even greater rise in the tissue pressure, caused by an increase in venous pressure, due to an arm band exerting a pressure of 40 mm. of mercury, demonstrated an increased permeability of the capillaries.

The following observations indicate that in normal pregnant patients the water and salt metabolism is abnormal, and that the renal function is altered, if not actually temporarily impaired. These changes in physiology in normal pregnant patients require but little added alteration to become pathologic. Once edema forms, a vicious circle has been started, which may terminate in the development of eclampsia.

Slemons noted that the ratio of urine to ingested fluids was less during pregnancy than in the puerperium or in the normal individual.

Holtermann found that 25 per cent of the pregnant women without edema, who were tested with Kaufmann's method, showed latent edema. He concluded that the latent edema in these women was not due to heart disease, but to an increased permeability of the capillaries.

Theobald and Verney have stated that pregnant women near term secreted more urine at night than during the day, but that when these women remained in bed the output of urine was constant. Animal experimentation demonstrated that the upright position favored the stagnation of blood in the lower extremities, due to gravity and the absence of muscular contractions. This stagnation leads to an increase in venous and capillary pressure and, consequently, to loss of fluid. Thus, late in pregnancy the fluid which filters into the tissues of the legs during the day, re-enters the circulation and is excreted at night. They state that if the fluid which escapes into the tissues by day is excessive and is not presented to the kidneys for secretion by night, edema of the tissues, commencing in the lower extremities, will occur.

Janney and Walker have noted that the pregnant patient at term excretes approximately 67 per cent of the usual normal output of ingested water. After delivery the excretion soon increases to 100 per cent. In a small series of toxemic patients, the excretion dropped to 17 per cent of the normal. These observers also found that the kidneys were far more efficient with the patient in the horizontal than in the vertical position.

We have confirmed their findings in a small series of normal patients at term. A group of toxemic patients showed an even more marked oliguria. In many instances the patients secreted no urine for the first hour of the test.

Sondern and Harvey have observed in normal pregnancy that after phenolsulphonephthalein injection the time for the appearance of the dye was increased and the average two-hour excretion was decreased.

We have noted that the mean for the urea clearance is 102 per cent before, and 125 per cent after delivery, and that the normal pregnant woman is able to excrete urine with an average specific gravity of only 1.022 after a fifteen-hour fast. The average specific gravity increases to 1.030 after delivery. The low specific gravity in pregnancy is due to a decreased amount of solids, especially urea and chlorides. All specimens of urine obtained on admission from 26 patients with eclampsia

were concentrated and highly colored, but contained an average concentration of sodium chloride of only 0.185 per cent. In 12 patients with pre-eclampsia the average concentration of sodium chloride was 0.169 per cent. The urea nitrogen was also usually less than 500 mg. per cent.

The excretion of large amounts of ingested sodium chloride or of potassium chloride are delayed in normal individuals. Torbert and Cheney found that the daily ingestion of 50 Gm. of sodium chloride for two days resulted in a decrease of 10 per cent in the hematocrit, and 15 per cent in the serum protein concentration in one subject. The colloid osmotic pressure decreased 39 per cent in one, and 31 per cent in the other subject. On the second day, edema of the face and ankles was noted.

Rupp found that the excretion of sodium chloride is delayed in pregnant women, and that the excess chloride is stored in the tissues, which appear to have an unusual affinity for it. He reports that there may be a dry retention of chloride and for that reason he advises a restriction of chloride rather than of fluids. Rupp believes that there must be some alteration in the capillary permeability and states that it is really the sodium ion which is the active agent in causing the edema.

Lundin and Scharf state that the salt and water metabolism are connected inseparably, both in normal and in pathologic conditions. They note that the administration of large amounts of sodium chloride caused a comparatively small sodium chloride retention in normal sheep, but a marked retention occurred in pregnant sheep.

Harding and Van Wyck have demonstrated that the daily ingestion of 15 Gm. of sodium chloride by a normal nonpregnant or pregnant woman results in a large positive water and salt balance. The weight increases and the serum proteins decrease in the concentration. Slight edema may occur. Similar therapy in a group of toxemic patients, whose edema had subsided on a salt-poor diet, resulted in a return of the edema in all of the patients, and an increased blood pressure and the recurrence of blurred vision and headache in some. The intravenous injection of 300 c.c. of a 10 per cent solution of sodium chloride had no effect on the normal pregnant woman, but in the borderline or mild toxemic patients it caused a rise in the blood pressure and a marked increase in the proteinuria. In an eclamptic patient, it caused a recurrence of the eclampsia. They conclude that excessive amounts of sodium chloride are definitely injurious to toxemic patients. They stated that a salt-poor diet is of great importance in the treatment of pre-eclampsia, and advised that the diet of normal pregnant patients should be salt-poor every fourth week as a prophylaxis against the development of pre-eclampsia.

Thompson and Pommerenke carried out a very careful water and electrolyte balance in three pregnant women. They found an average retention of sodium amounting to 14.7, and of potassium amounting to 7.9 milliequivalents. The chloride balance in one patient was 1.2, in the second it was 4 milliequivalents, and in the third it was negative. They noted a very close parallelism between the chloride and sodium balance. The potassium balance varied less than sodium or chloride, and there was no correlation between sodium and potassium.

Freyberg and his co-workers studied the caloric intake, nitrogen, water, and sodium balance of a patient during the last two months of pregnancy. They found that the sodium balance was positive for almost every day of the test, and the retention ranged from 0.132 to 0.22 Gm.

Coons and her co-workers report a daily mean retention in normal pregnant patients of 0.877 Gm. of chlorine, 1.265 Gm. of sodium, and 0.508 Gm. of potassium.

Thorn, Nelson, and Thorn have found that there is a retention of water, sodium, and chlorine in women at the intermenstrual and premenstrual periods, when the

level of the sex hormones is high. They also found that estrone, administered to dogs, caused a water retention and an increased elimination of potassium.

Taylor and his co-workers have studied the sodium and potassium balances and the excretion in the urine of prolan, pregnanediol, and the estrogens, in 4 normal pregnant patients and 2 pre-eclamptic patients. They concluded that sodium is retained in pregnancy and the puerperium during a high estrogen concentration, and is lost during periods of diminishing hormone concentrations. There was no correlation between the potassium balance and the hormone level. It is interesting to note that the patients showed a maximum sodium and potassium excretion about the second to the sixth day of the puerperium. Our findings are similar, indicating that there has been a marked storage of electrolytes in the extracellular fluids. One patient showed a marked negative balance in the ante-partum period, as we have also demonstrated repeatedly. Our criticism of Taylor's work is that he compares exact measurements of the total sodium and potassium intake and output with the approximate determination of the hormones in the urine. They assume that the excess of hormones in the urine is due to an overproduction, but the same factor, or factors, concerned in the negative electrolyte balance may also account for the marked excretion of the hormones. In other words, we have noted that not only are sodium and chlorine retained in the edema fluid, but that urea, phosphate and other metabolic products are stored in the fluid. It is just as reasonable to believe that the hormones also may have been stored in the tissue fluids and that the correlation is accidental.

Taylor and his co-workers, in a recent extensive study of hormonal changes in pre-eclampsia and eclampsia, have reviewed the literature and have concluded that: "The tests for these hormones give only approximate values. The blood and urinary figures for these substances show large normal variations when different individuals are compared and even when different specimens of the same individuals are contrasted. The hormonal changes observed in the toxemic patients are perhaps associated with the cause of the toxemia, but may simply be the result of the disturbance of kidney, liver, or placental physiology."

Improper nutrition, anemia, and hookworm disease favor the formation of edema. We have had a number of edematous pregnant patients with hemoglobins of from 3 to 8 Gm. per cent, in whom the edema disappeared if the hemoglobin was increased to 11 Gm. per cent by blood transfusion. All of these patients had serum protein concentrations above the edema level and, with the exception of several with a borderline hypertension, were otherwise normal. Balfour stated that 2.93 per cent of the natives delivered in his hospital in India had a severe anemia, characterized by fever, tachycardia, gastrointestinal disturbances, albuminuria, and edema.

Wickramasuriya stated that the incidence of toxemia was increased in the Hindu with anemia due to hookworm disease. Ross and his co-workers at Duke University report that their patients with edema and eclampsia have had a diet markedly inadequate in proteins, and some had low serum protein concentrations. Arnell, at the Louisiana State University, states that he has observed true nutritional edema in pregnant patients, but that marked edema, as a complication of hookworm anemia, is more common. The incidence of toxemia in the patients of this latter group is not materially increased.

The ante-partum hematocrit figures for edematous patients with pre-eclampsia, eclampsia, and vascular-renal disease are 37.4, 44.0, and 37.0 volumes per cent; and the post-partum figures are 38.1, 38.4, and 39.8 volumes per cent, respectively. The mean hematocrit figures for normal pregnant patients at term are 37.3 ± 4.2, corresponding to a hemoglobin of 11.6 Gm. per cent. Therefore, anemia was not a factor in causing edema in our toxemic patients.

Leiter and Fahr, and Kerkhof and Giere have demonstrated that edema will not develop in dogs with serum protein concentrations of 3 to 4 Gm. per cent, unless the animal is given adequate amounts of sodium chloride and water. Observations at various clinics indicate that the edema of pre-eclampsia or eclampsia may be, as a rule, cured by eliminating from the diet one of the chief constituents of edema fluid, namely, water, sodium, or chloride. The consensus of opinion is that the curtailment of sodium chloride presents fewer difficulties and causes less discomfort to the patient than the restriction of water.

Arnold believes that eclampsia and pre-eclampsia are due to cerebral dysfunction, caused by an abnormal retention of water. He dehydrates his eclamptic patients by restricting the fluid intake, by administering saline cathartics, by repeated spinal drainage, by the intravenous injections of hypertonic glucose solution, and by venesection. The pre-eclamptic patient is treated by restricting the fluid intake and by the use of a low salt diet.

Jerlov, in a large group of toxemic patients, finds that the restriction of salt is the most important dietary precaution in both preventing and treating toxemia. He also restricts meat to two or three times per week in toxemic patients, and advises boiling the meat rather than roasting it.

De Snoo states that he has been able to almost eliminate eclampsia from patients in his clinic by the use of a salt-poor diet. He also follows the urinary output of chloride for its prognostic value.

Bland and Bernstein found that in pre-eclamptic toxemia the blood pressure is not influenced by bed rest and a regular diet. A salt-free diet resulted in a decrease in the blood pressure in all cases. The chloride excretion in the 24-hour urinary output served as a criterion for treatment. The success of their treatment depended upon maintaining the urinary chloride below 1 gm. A salt-free diet led to the disappearance or amelioration of all the symptoms or signs and to a marked loss in weight.

We have been using a salt-poor diet in the treatment of toxemia of pregnancy, with excellent results. Our sodium chloride balance studies were started in 1926. The intake of sodium chloride, to be of any therapeutic value, must be restricted sufficiently so that the twenty-four-hour excretion of sodium chloride in the urine is less than 3 Gm. Our low sodium chloride diet contains 0.715 Gm. of sodium, 1.42 Gm. of chloride, 2.61 Gm. of potassium, 0.95 Gm. of calcium, 1.47 Gm. of phosphorus, 62 Gm. of protein, 76 Gm. of fat, and 229 Gm. of carbohydrate. The eclamptic diet, consisting of fruits and fruit juices, contains 0.74 Gm. of sodium, 1.69 Gm. of potassium, 1.06 Gm. of chloride, and is used for a period of from five to seven days.

Strauss stated that in edematous pregnant patients the calculated colloid osmotic pressure and the total plasma proteins were decreased, and concluded that the latter was due to a low protein intake. He stated that the edema disappeared if the patient was given an adequate amount of protein, vitamin B, liver extract, and a sodium-poor diet. Three of his patients with hypoproteinemia and edema in the first pregnancy developed low serum protein concentrations in the next pregnancy, despite a high protein intake. They did not, however, develop edema because they were kept on a salt-poor diet. In his last paper he stated that the loss of weight in edematous patients occurred without any change in the plasma protein level and was initiated by the administration of a diet low in sodium.

Tillman, discussing Strauss' work, stated that he was not in agreement that the edema was responsible for the toxemia of pregnancy, and that he has repeatedly seen edematous pre-eclamptic and eclamptic patients with normal serum protein concentrations.

Stander, discussing Strauss' paper, stated that in his belief a lowered serum protein is not the cause of edema in pre-eclampsia and eclampsia.

Zangemeister was the first to describe the abnormal retention of water in pregnant women (hydrops gravidarum), which was associated with albuminuria and convulsions in a few cases.

Fink, in 1921, discussed hydrops gravidarum and stated that it was possible for edema to be present without an increase in the blood pressure or kidney findings. The formation of edema, according to him, was favored by the intake of salt and acid foods. He does not believe that the subcutaneous tissues maintain a strict isotonicity, as does the blood, and that excess sodium chloride may be stored. He believes that eclampsia is due to cerebral edema.

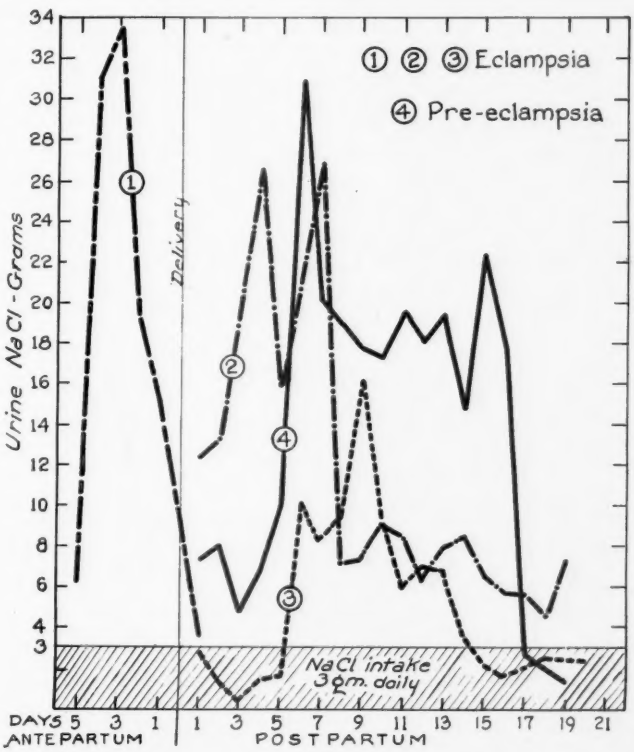

Fig. 1.—Patient 1: Negative sodium chloride balance of 99 Gm. (equivalent to 16 kilograms of water), with loss of 9 kilograms in weight. Patient 2: Loss of 164 Gm. (equivalent to 27 kilograms of water), with loss of 50 kilograms in weight. Patient 3: Loss of 37 Gm. (equivalent to 6 kilograms of water), with loss of 20 kilograms in weight. Patient 4: Loss of 204 Gm. (equivalent to 34 kilograms of water), with loss of 41 kilograms in weight.

Heynemann believes that the capillary damage is of major importance in causing eclampsia. He ascribes the edema to an increased permeability of the capillaries, but does not know the primary cause for the damaged capillary endothelium.

In Fig. 1 we have presented data on three eclamptic patients and one pre-eclamptic patient. Each patient had a tremendous negative chloride balance, a marked diuresis, and a marked loss in weight. There is some correlation between the amount of chloride excreted and the weight lost. For example, Patient 4, who had a negative sodium chloride balance of 204 Gm., corresponding to 34 kilograms of water, lost 41

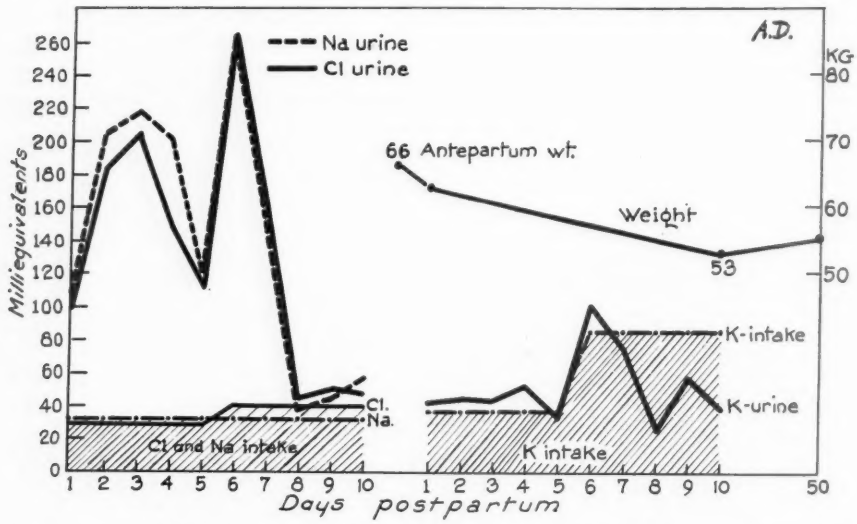

Fig. 2.—Graph of patient on eclamptic diet for first five days, and on a low sodium diet for the next five days. Fetus weighed 2,000 Gm., and the amniotic fluid and placenta were assumed to have weighed 1,000 Gm., giving a total weight loss of 3,000 Gm. at delivery.

$$\text{Milliequivalent} = \frac{\text{Grams of electrolyte}}{\text{Molecular weight of electrolyte}} \times 1{,}000.$$

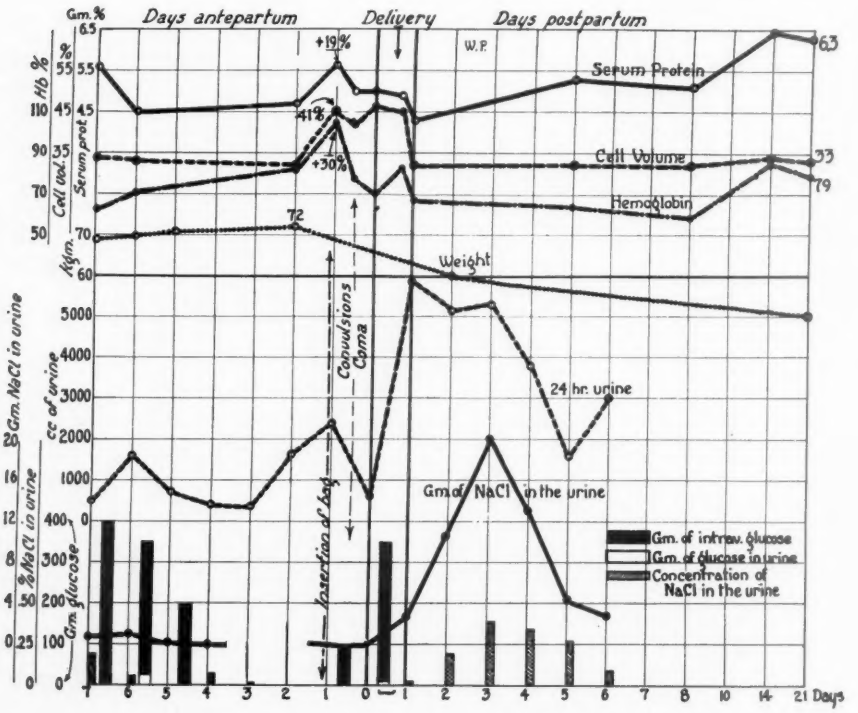

Fig. 3.—Graph illustrating the changes in the chloride and water balance, weight, serum protein, and hematocrit in a pre-eclamptic patient who did not respond to treatment and who ultimately developed eclampsia. The retention of chloride, as demonstrated by its absence from the urine, and the simultaneous gain in weight are noteworthy.

kilograms in a period of nineteen days. The loss in weight and the water loss, calculated on the sodium chloride excretion, do not coincide. Experiments are now in progress to determine if a better correlation occurs between weight loss and measurements of the extracellular body water. However, no potassium determinations were made on these patients, and, although the edema is presumably extracellular, we believe that the muscle cells may share in the abnormal retention of water in some patients.

A large amount of water could be held in the muscle cells of the body without the patient showing any demonstrable edema. This phenomenon would account for those patients whose weight gain is so rapid that it must be due to a retention of water and yet no edema can be detected. Furthermore, if this water were quickly released from the cells, it would account for the sudden appearance of edema noted in many eclamptic patients, and for the occasional development of symptoms and signs of acute cardiac decompensation in toxemic patients. We hope that further balance studies of sodium, potassium, and chlorine, and the determination of the extracellular body water may help us to determine if intracellular edema can occur.

We have noted that the potassium excretion usually parallels the chloride and sodium excretion as long as they are negative. This is illustrated in Fig. 2. The chloride and sodium excretions usually parallel each other, and in this patient they were almost identical. The negative balance for these substances indicated that there had been considerable retention. The chloride excretion was equivalent to 9 kilograms of water, and the patient lost 10 kilograms. The negative potassium balance may have been due either to a washing out of potassium along with the sodium, or to an intracellular edema. Similar studies on other patients yield identical results.

Fig. 3 illustrates a sodium chloride retention despite the diet, bed rest, and intravenous injections of hypertonic glucose solution. The urine became chloride-free and the weight increased markedly. Labor was induced, but no precautions were taken to prevent a blood concentration, and eclampsia developed. The chloride and water excretion were marked after delivery and the weight decreased 12 kilograms in twenty-one days.

Fig. 4 is presented to illustrate the relationship between edema, the clinical findings, and the changes in the serum protein concentration and the cell volume. With a low sodium diet we were able to produce a marked negative balance of sodium chloride, associated with a weight loss of 8 kilograms in a period of nine days. During this time a blood dilution occurred, with the serum protein concentration decreasing to 5.1 Gm. per cent at about the height of the diuresis. Coincidental with the negative chloride balance, the edema diminished and the blood pressure also decreased. The blood became concentrated at the time of delivery, and in the post-partum period there was a second dilution during the diuresis.

Analyses of the twenty-four-hour specimens of urine from edematous post-partum patients for inorganic ash, total base, phosphate, nonprotein

and urea nitrogen, and titrable acidity reveal that the excretion of these substances roughly parallels the excretion of sodium and chloride, indicating that the edema fluid also contained these various substances.

Some patients gain weight excessively in each pregnancy and may develop edema, but, as a rule, no other symptoms or signs appear. We have studied these patients over a period of years, and they have always had normal blood and urine findings and a normal renal function. It is obvious that these women have difficulty in excreting sodium chloride because they do not gain excessively on a rigidly controlled sodium-poor diet.

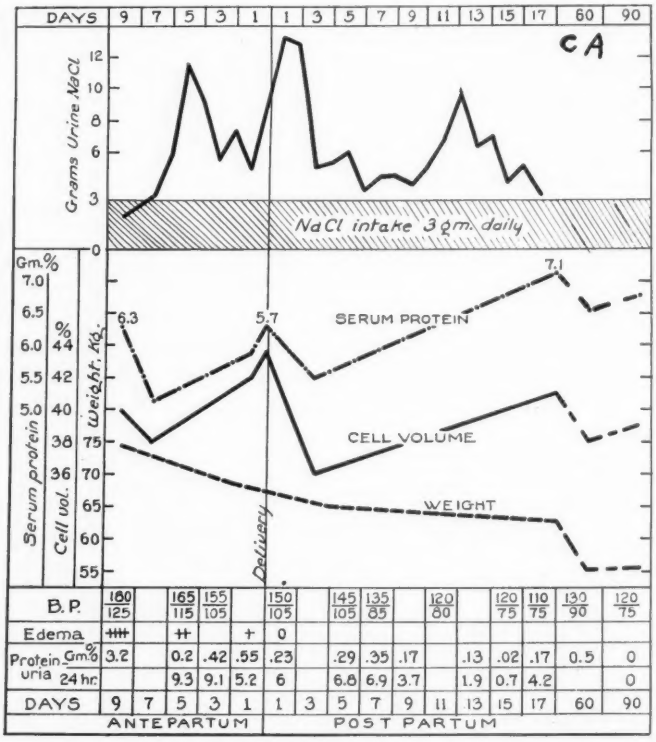

Fig. 4.—Graph depicting the typical ante-partum and post-partum changes in serum protein, hematocrit, chloride excretion, edema, blood pressure, and weight loss in a patient with pre-eclampsia. The marked ante-partum excretion of chloride and clinical improvement indicate the beneficial effects of bed rest and a proper diet.

That pregnancy has a very definite effect on capillary permeability and water balance is exemplified by studies of two pregnant patients with diabetes insipidus who, despite their polyuria, showed excessive gains in weight and developed pretibial edema and a mild hypertension. Their serum protein concentrations were 6.5 and 5.5 Gm. per cent, respectively, at the height of the edema.

CONCLUSIONS

The following physiologic changes occur in normal pregnancy:

1. The venous pressure in the legs is increased and causes an increased loss of fluid from the blood into the tissues of the legs.

2. There is an increased capillary permeability.

3. The elimination of water and solids by the kidney is delayed or impaired.

4. The average serum protein concentration is 6.5 Gm. per cent.

5. The average colloid osmotic pressure of the serum protein is 28.7 cm. of water.

Pre-eclampsia and eclampsia may occur if these changes are of greater magnitude than normal, or if they are exaggerated by internal or external factors. Thus we find the following in these diseases:

1. Greater alterations than normal in the venous and capillary pressures and capillary permeability.

2. The average serum protein concentration in edematous patients with pre-eclampsia is 6.22, with eclampsia it is 6.7, and with vascular-renal disease and normal renal function it is 6.67 Gm. per cent.

3. The average colloid osmotic pressure of edematous pre-eclamptic patients is 24.9, and of toxemic patients without edema it is 26.5 cm. of water.

4. The retention of sodium, chlorine and water is greatly increased in some pregnant patients, resulting in an abnormal gain in weight, and, finally, in demonstrable edema.

5. Changes in the concentration of the female hormones are apparently associated with edema, but whether this is the cause or the result cannot be stated from our present knowledge.

6. The prevention and treatment of edema are dependent on the limitation in the diet of the principal components of edema fluid, namely, sodium chloride and water. The curtailment of sodium chloride in the diet presents fewer difficulties and causes less discomfort to the patient than the restriction of water.

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URINARY INCONTINENCE RELIEVED BY RESTORATION AND MAINTENANCE OF THE NORMAL POSITION OF THE URETHRA*

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INTRODUCTION

A VERY sharp distinction must be made between urinary incontinence and urinary urgency or frequency lest we operate upon a patient with urgency and frequency who has no incontinence and find that after operation she still presents these symptoms but is really continent. We must keep the confidence of, and be frankly honest with, a patient having incontinence. We should clearly explain to her that sometimes the first operation may be unsuccessful and a second will be required. I hope to make the reasons for the above remarks clear. This paper is a presentation of a few facts and experiences which I have acquired since my previous publications[1-3] have appeared. By noting my failures and mistakes and studying carefully the histology, it has been possible to report progress and, at the same time add more clarity to the problem.

It has been shown by Goff[4] and clearly confirmed by me that the bladder and ureters (including the trigone) lie loosely upon the vaginal wall, while the urethra lies in very intimate contact with the anterior vaginal wall. Microscopic cross section shows the levator mus-

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cle fibers (Fig. 1) originating from the periosteum of the symphysis near the midline do not pass beneath the urethra but pass posteriorly and insert their ends into the lateral wall of this part of the vaginal cuff, thus creating the "dimple" of the vestibule. The anterior vaginal wall consisting of smooth muscle fibers intermingled with connective tissue passes below the urethra from the region of one "dimple" to the opposite "dimple." The vaginal wall extends from one end of the urethra to the other in intimate contact with the outer coat of the intrinsic structure of the urethra. The vaginal wall thus constitutes a table on which the urethra rests in intimate relationship. This fact has been utilized with satisfactory result in one case, described further on in the paper.

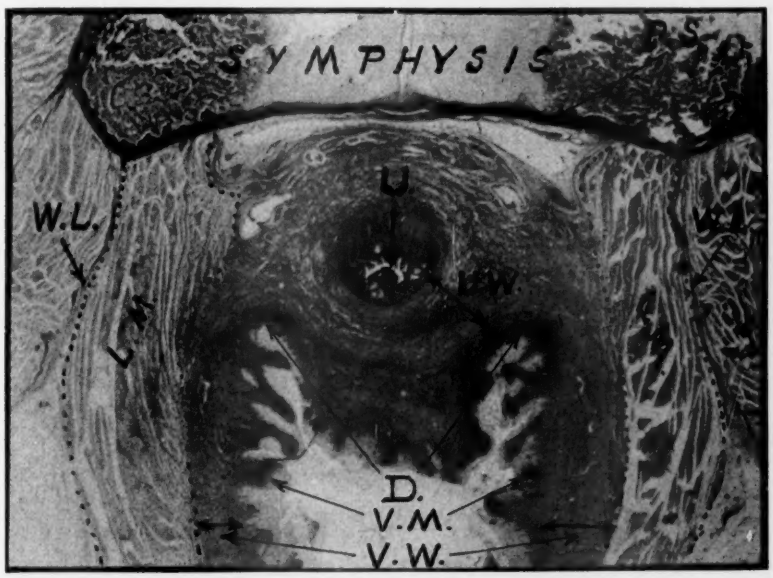


Fig. 1.—Photograph of a microscopic section cut at right angles to the urethral canal, through the urethra, vagina, and the symphysis, to show the vagina and insertion of those levator fibers nearest the midline. *U.*, urethral canal and mucosa; *U.W.*, urethral wall; *D.*, "dimple"; *V.M.*, vaginal mucosa; *V.W.*, vaginal wall; *W.L.*, white line; *P.S.*, periosteum of the symphysis; *L.M.*, levator muscle (within the dotted area). Note (1) the origin from the periosteum of the symphysis and from the white line, and the insertion into the walls of the vagina; (2) the arrangement of muscle and vaginal wall to form the dimple; (3) note that none of the levator fibers pass beneath the urethra.

THE NORMAL URETHRA

The normal urethral mechanism in action can be studied with the aid of radiographs, and from these a comparison of the damaged urethra is made possible. Two hundred cubic centimeters of a 3 per cent solution of sodium iodide are instilled into the bladder. The sac, to outline and distend the urethra, is put in place and connected with a manometer containing 25 per cent solution of sodium iodide, and the manometer raised so that its fluid level is 30 cm., or 12 inches above the urethra when the radiograph is taken. While a radiograph is being taken, the patient lies on her back (or side, for lateral views) and is

asked to "hold," to "relax," or to "void" as the case may be. In this article "relaxing" means that the patient directs no exertion upon the bladder or urethra but lies perfectly still; "holding" means that she uses all her voluntary efforts to prevent urine from escaping from the urethra; and "voiding" that she uses all her voluntary efforts to force urine from the urethra. Fig. 2 is a composite picture of a radiograph of the normal bladder and urethra while "voiding," superimposed upon a radiograph of the same taken while "relaxing." One notes, when in the "relaxed" state, the small amount of dilatation of the sphincter surrounding the internal meatus, the normal position of

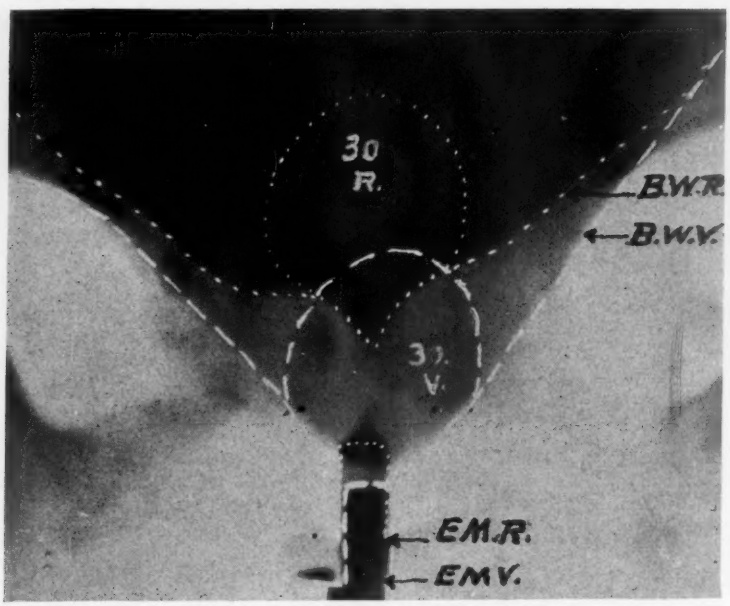


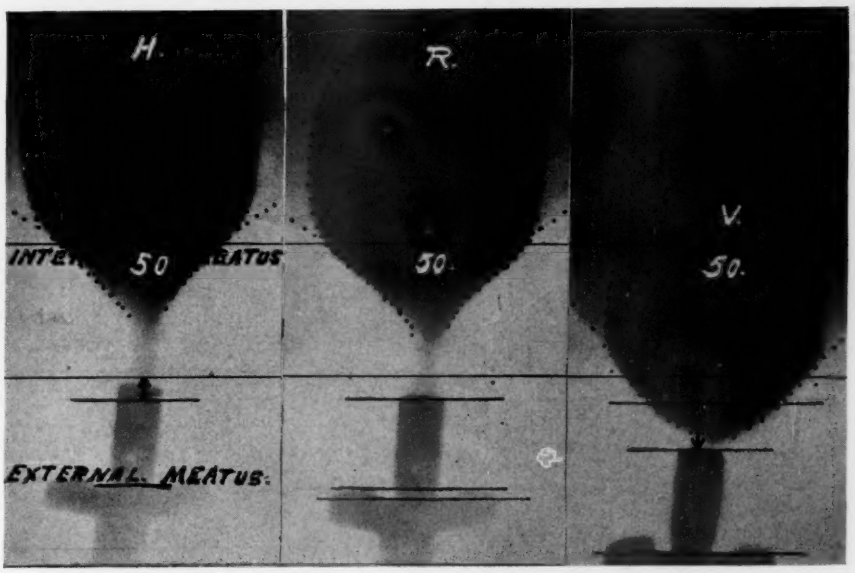
Fig. 2.—The normal urethra in the "relaxing" and "voiding" state (composite picture by superimposing two radiographs). *30 R.*, The sac outlining the urethra and bladder in the "relaxing" state; *30 V.*, the sac outlining the urethra and bladder in the "voiding" state; *B.W.R.*, bladder wall, "relaxing;" *B.W.V.*, bladder wall, "voiding;" *E.M.R.*, external meatus, "relaxing;" *E.M.V.*, external meatus, "voiding."

Note: In the "voiding" state (1) the bladder floor is pushed down between the rami; (2) the inner part of the sphincter is dilated; (3) the urethra is pushed out of the pelvis; (4) the position and shape of the urethra permit all the urine to escape from the bladder.

Note: When incontinence is present, the urethra and bladder in the "relaxing" state will assume some permanent position between the two positions shown above. Greater incontinence will exist the nearer the extreme "voiding" state is approached.

the floor of the bladder, and the position of the external meatus relative to the symphysis. In the "voiding" state, by comparison, the bladder floor seems to have been pushed down between the rami, the inner half of the urethra dilates widely (in fact its diameter appears to be the same diameter as the sac, 2 cm.) while the outer half dilates very little, and the external meatus of the urethra has been pushed endwise out of the pelvis about 1 cm. Fig. 3 (anteroposterior view) is a radiograph illustrating the normal urethra in the "holding," "relaxing," and "voiding" states. In the "holding" position (Fig. 3, *A*),

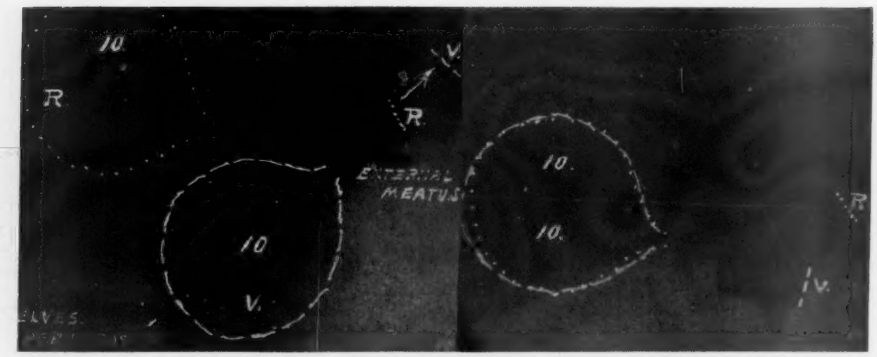
little deviation from the "relaxing" position occurs. The voluntary effort on the part of the patient does not pull the urethra far into the pelvis, nor does it much diminish the diameter of the sphincter about the internal meatus, but the external meatus is drawn about 1 mm. into the pelvis. On the contrary, the "voiding" position (Fig. 3, *C*) compared with "relaxing" position (Fig. 3, *B*) shows the sphincter about the internal meatus to be much dilated and the whole urethra to have been pushed endwise more than 5 mm. out of the pelvis. Fig. 4 (lateral view) is a radiograph illustrating a normal urethra in "relaxing" and "voiding" states. The distance the external meatus has been pushed



A. *B.* *C.*

Fig. 3.—Radiographs of the urethra and bladder, anteroposterior view normal urethra. *A*, In the "holding" state (*H.50*); *B*, in the "relaxing" state (*R.50*); *C*, in the "voiding" state (*V.50*). In the "holding" state, the sphincter about the inner third of the urethra is closed a little tighter and the external meatus is drawn a short distance within the pelvis as compared to the normal "relaxing" state. Hence, by position, one would say the "relaxing" state should function almost as efficiently as the "holding" state. Directly opposed to this in the "voiding" state, the sphincter about the inner third of the urethra is much dilated, the bladder is pushed in direction down and out of the pelvis and the external meatus is pushed nearly a centimeter out of the pelvis as compared to the "relaxing" state.

out of the pelvis while "voiding" varies with each patient, the one illustrated being about 1 cm. Another observation one makes is, that less than 1 cm. in length of the sphincter from the internal meatus takes part in the dilatation when "voiding." The urethra is pressed downward into the vagina along with the bladder. One interesting fact which is observed when the sacs are superimposed (Fig. 4, *B*) is that during "voiding" no fluid leaves the sac, although it is perfectly free to do so. One deduces from this that the fluid pressure in the bladder is not increased when voiding, but, that only the exit of urine is made easier. Fig. 5 (lateral view) illustrates the behavior of a large cystocele: First, when "relaxing," second (Fig. 5), when a



A. *B.*

Fig. 4.—Lateral view, normal urethra. *A*, Sac *10.R* showing position of urethra and bladder in the "relaxing" state and *R*, the position of the external meatus; sac *10.V* showing the position of the urethra and bladder in the "voiding" state, and *V*, the position of the external meatus. *Note:* (1) The bladder and the urethra have been pushed downward and forward into the vagina. (2) The closed portion of the urethra has been shortened about one-fifth in the "voiding" state and the remainder of the sphincter has dilated. (3) The external meatus has been pushed outward and downward from within the pelvis. *B* (Sacs in *A* superimposed). The sac does not change its size any appreciable amount in the "voiding" state.

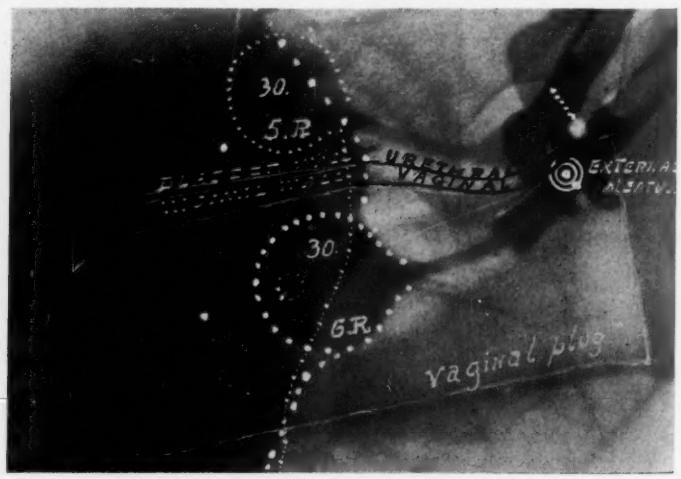


Fig. 5.—Two radiographs superimposed, lateral view, the urethral sphincter being only slightly relaxed. There was a very large cystocele which on straining would balloon out of the vagina. The first radiograph was taken in the "relaxing" state, sac *30.6R* outlining the relation of the bladder and urethra. The shaded portion represents the dilatation of the sphincter about the inner third of the urethra and the double circle the external meatus. The second radiograph was taken in the "relaxing" state with a Sim's vaginal plug in the vagina, sac *30.5R* outlining the relation of the bladder to the urethra, and the line of dots above the double circles indicate the external meatus. The Sim's plug has lengthened the urethra, the external meatus being more external to the pelvis and the internal meatus more internal. The sphincter about the inner third of the urethra appears completely closed. The urethra and bladder have been raised in the pelvis. These are the requisites for continence. The Sim's plug has effected a lengthening of the urethra, by what means it is impossible to say. This lengthening theoretically should greatly increase the sphincteric power of control.

Note: The lines between "bladder wall" and "vaginal wall" indicate the plane which the bladder and the urethra rest upon when the Sim's vaginal plug was in the vagina.

Sims' vaginal plug is inserted in the vagina, and third, when "voiding" (Fig. 6). This patient had a mild incontinence, losing a drop or two of urine only when coughing or sneezing. The features presented by this are (1) that the sac contains less fluid when the bladder is high, hence the urethra is longer and the internal sphincter is more tightly closed; (2) that the middle and inner thirds of the urethra in the "voiding" state can be turned through an angle of 90 degrees to lie between the labia and the sphincter mechanism can continue to function in this position; (3) that in "voiding" this urethra is pressed endwise out of the pelvis about 0.5 cm. Since there is comparatively

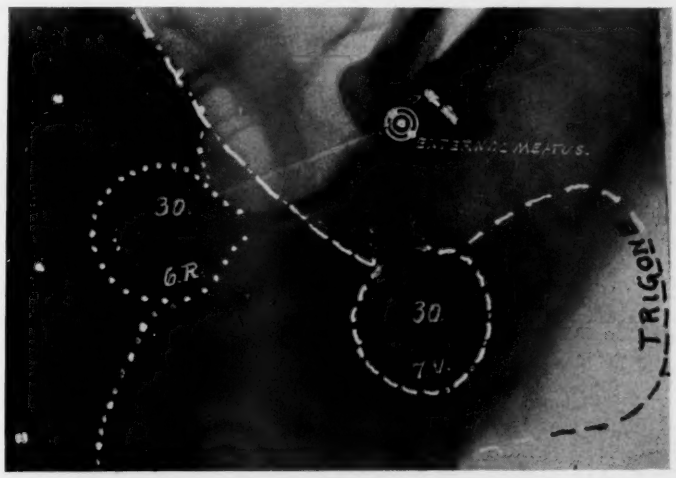


Fig. 6.—Two radiographs superimposed, lateral view; same patient as in Fig. 5. The first radiograph was taken in the "relaxing" state, sac *30.6R* outlining the relation of the bladder to the urethra. The shaded portion represents the dilated portion of the sphincter about the inner third of the urethra, the double circle the external meatus. The second radiograph was taken in the "voiding" state, sac *30.7V* outlining the relation of the bladder and urethra, and the dashes the external meatus. The urethra has become angulated, the inner half having turned through 90° from the "relaxing" state. The external urethra has been pushed almost 0.5 cm. out of the pelvis. The length of the urethra is about the same as in the "relaxing" state, therefore, there is still continence. The bladder and part of the trigone lie outside the vagina. Where the ureteral orifices are cannot be conjectured. The urethra itself has scarcely assumed any of the "voiding" state contour, a fact which coincides with the difficulty encountered in voiding by a patient with a protruding cystocele.

little support from the vaginal wall beneath the urethra, we must consider that there is little or no sphincteric control offered by the support, and practically complete control is in the intrinsic sphincter mechanism.

URETHRAL STATE AND INCONTINENCE INTIMATELY RELATED

Since the normal urethra in the "relaxed" state at all times maintains its contour and position and prevents any urine from escaping from the bladder, and the same urethra in the "voiding" state permits all the urine to run out of the bladder, one can deduce that the patient with incontinence has a urethra with some permanent degree of the "voiding" state. Now, (1) the continuous loss of sphincter muscle tone or the permanent distortion of that portion of the sphincter muscle surrounding the inner third of the urethra produces various degrees of the permanent

voiding state and must always be present for incontinence, while (2) a vaginal wall which has stretched below the bladder and urethra and (3) a urethra which has been moved more external to the pelvis may or may not be present. Loss of sphincter muscle tone may appear with increasing age, and relaxation may be responsible for incontinence in a nulliparous woman.

FACTORS CONTRIBUTING TO INCONTINENCE

A number of factors have been previously mentioned and will not be repeated here. Cases are briefly cited to illustrate other contributing causes:

CASE 1.—A patient having urinary urgency and frequency, and doubtless some degree of incontinence, was referred by her general practitioner to a urologist. By cystoscopic examination the urologist found a few urethral polyps, and he removed them by electrocoagulation. From this time on, the patient had a persistent incontinence.

CASE 2.—Another patient, referred to a urologist, had a number of urethral caruncles which he vigorously cauterized. The result was a marked intermittent incontinence persisting for several months.

CASE 3.—Another patient, about 55 years of age, unmarried, had a pelvic cellulitis, probably followed by bladder and urethral adhesions as a child, and developed a severe constant incontinence for several months.

CASE 4.—A patient, married, nulliparous, about 58 years of age, had a constant moisture from the vagina, diagnosed by two gynecologists as hydrorrhea, but a third gynecologist diagnosed the condition as one of incontinence with a relaxed vesical sphincter developing several years before operation.

CASE 5.—Another patient, after a plastic operation for moderate lacerations and mild incontinence had a large mushroom catheter jerked from her urethra on the eighth postoperative day by an interne, and she became markedly incontinent.

CASE 6.—Another, a young woman, delivered a medium-sized baby after a five-hour labor terminated by forceps. She became persistently incontinent. The cause, here, was a urethrovaginal fistula at the junction of the middle and inner thirds of the urethra, associated with a lateral distortion of the inner third of the urethra by a dense band of scar tissue pulling the inner third of the urethra over to the right ramus. Three operations had been done upon this patient before I saw her.

CASE 7.—In a multiparous patient with moderate lacerations of the anterior and posterior vaginal walls I did a Kelly operation for incontinence together with an operation for cystocele, rectocele, and laceration of the pelvic floor which was a failure. Incontinence was worse than before.

CASE 8.—A multipara with some prolapse, extensive cystocele, and rectocele had marked incontinence for years. Trauma at labor was the cause of her incontinence.

TRAUMA OF LABOR

As the size of the fetus and uterus increases, the space for the bladder between the symphysis and the uterus correspondingly diminishes. The bladder can take care of this physiologic condition in two ways, either by a frequent emptying of itself, or, by lateral distention into the paravesical spaces (the latter can be seen by radiographic study

of the bladder). The lower uterine segment broadens laterally, but there may be little change in the size of the anterior vaginal wall. The bladder and ureters lie loosely upon this floor of vaginal wall.

Labor sets in, the cervix dilates, and the anterior vaginal wall is stretched laterally to some degree as the head descends. In some instances the head produces a contusion of the bladder and the anterior vaginal wall, which on healing causes the bladder to become fixed to the vaginal wall, either on part or all of one side, or, in some cases almost completely. A second labor will then stretch both the bladder and the vaginal wall, and if this stretching is carried forward in the midline, the posterior urethra and bladder wall may become thinned out. If carried still farther along the floor of the bladder, the fibers of the urethra and the vaginal wall of the vestibule will be split, allowing the urethra to

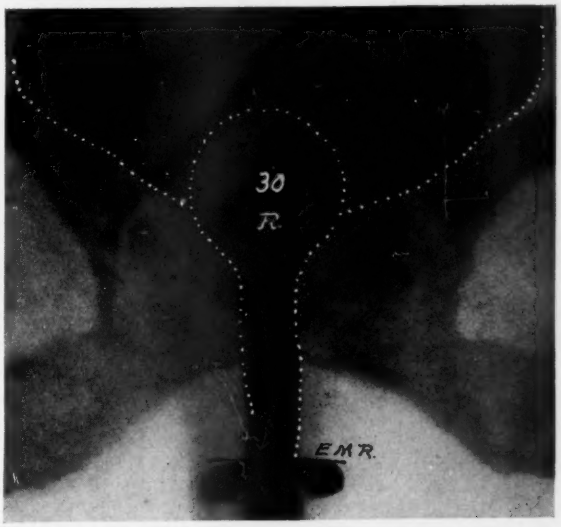


Fig. 7.—Radiograph, "relaxing" state, failure at operation, cause not known. *Note:* One sees here a marked relaxation of the sphincter mechanism from one end of the urethra to the other, several weeks following my operation. Dr. Daniel Mishell repeated my operation a few weeks later with complete success.

drop into the vagina and at the same time be pushed a short distance out of the pelvis. Should the damage be between the urethra and the ramus, its healing may leave connective tissue, permanently distorting the urethra. These urethras assume certain degrees of a permanent state of voiding.

FAILURES AND THEIR SOLUTION

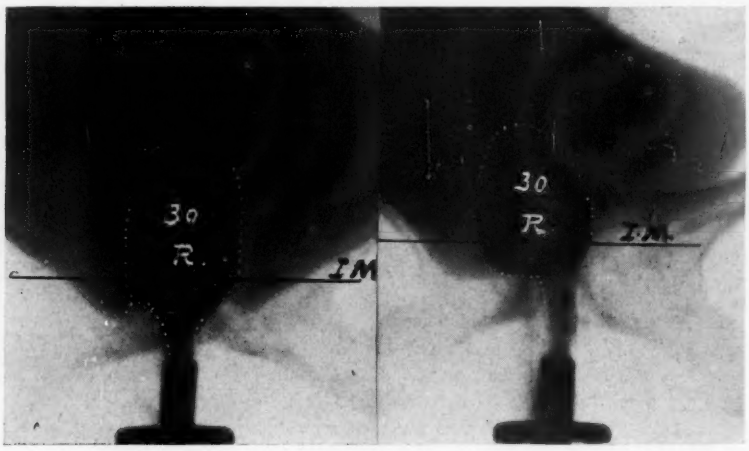
Failures have occurred and I have been able to get some valuable information from a careful study of them. The cases cited serve to illustrate:

CASE 1.—A patient, 55 years of age, unmarried, was found to have extensive adhesions between the bladder and the vaginal wall, between the urethra and bladder and both rami. My method of operation was done, but the patient was still incontinent. Fig. 7 shows the bladder to be in good position; there is some dilatation of the inner third of the urethra and a marked dilatation of the middle and

outer thirds of the urethra. The reason for the failure is not known but it is different from other cases. Repetition of my operation by Dr. Daniel Mishell resulted in normal control.

CASE 2.—Another patient with cystocele, some prolapse, a rectocele, and lacerated pelvic floor who had a plastic operation which included my technique for incontinence, unfortunately had a moderate infection of the anterior wall as a postoperative complication. Fig. 8, *A*, shows the fall of the bladder wall and a marked dilatation of the sphincter about the inner third of the urethra. There was a bilateral failure of maintenance following restoration. This patient has not been reoperated upon.

CASE 3.—A patient, 25 years of age, was delivered four years ago of a 7½-pound child in a five-hour labor terminated by forceps. She lost control of her urine from that time on. She does not know whether she had a damaged bladder or urethra. An attempt was made three months later to restore continence without success. Two later attempts by a urologist also failed. Whether the original incontinence was due



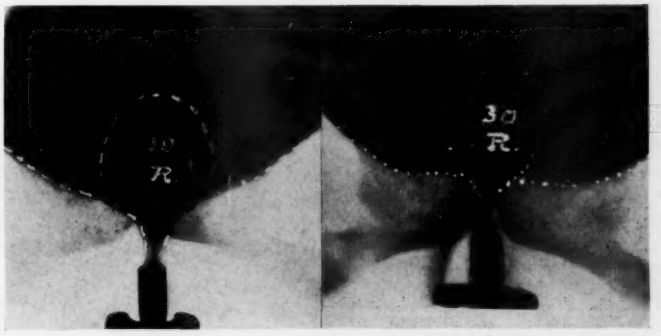
A. *B.*

Fig. 8.—Failures at operation. *I.M.*, internal meatus. *A*, Radiograph of a urethra and bladder following my operation. There was a postoperative infection in the anterior vaginal wall. The urethra and bladder walls probably returned to their original preoperative positions. Restoration was accomplished without maintenance. This shows a bilateral failure of maintenance. *B*, Radiograph of a urethra and bladder following my operation. The right border of the trigone had to be separated from the right ramus by sharp dissection, during which procedure the bladder was entered. Restoration was accomplished but infection set in. The right urethra and bladder returned to the position which they occupied before operation. This shows a unilateral failure of maintenance.

to a urethrovaginal fistula, is not known, but probably it was. The pediatrician taking care of the child referred her to me. A fistula, about 2 mm. in diameter, having its opening into the vestibule of the vagina about 1 cm. to the right of the midline and 2 cm. from the external meatus, made its way backward and medially in an oblique course into the urethral canal by an opening about 1 cm. from the internal meatus. A ureteral catheter was passed through the fistula into the bladder. During withdrawal a cystoscope was used to follow the end of the ureteral catheter to the internal meatus, and a urethroscope to follow it until it disappeared. The opening was located about 1 cm. from the meatus. Hence, about 1 cm. in width of the sphincter of the inner third was beyond the fistula. This portion of the sphincter, if normal, should have prevented urine from escaping through the fistula when the patient was recumbent. But she was always wet. Therefore, this portion of the sphincter was inefficient. The cause, found during dissection, was a dense scar about 1 mm. thick and 4 mm. wide, holding the wall of the urethra well over to the right ramus posterior to the fistula. This patient had both a fistula and a distorted urethral sphincter. Had only the fistula been excised and closed, the patient

would not have been relieved. The fistula was dissected out, its opening closed to evert the urethral mucosa into the canal, the scar band cut, the urethra completely freed from both rami and my incontinence operation completed. The patient now has normal control of her urine. One must conclude that the liberal or complete dissection is the conservative one, when the end result is our goal.

CASE 4.—In some cases the trauma of labor relaxes or disengages the normal support of the urethra, so that it assumes the position which the normal urethra takes during the act of voiding. One such patient had a normal dissection of the vaginal wall from the urethra and the bladder, extending over to the ramus pubis on each side, and Kelly sutures were placed. She had more incontinence



A. *B.*

Fig. 9.—*A*, Radiograph of a bladder and urethra following a Kelly operation resulting in failure. *B*, Radiograph of the same bladder and urethra following my operation some months after, resulting in success.

Note: The procedures in both operations were almost identical, except that in my operation separation of the bladder and urethra from both rami and replication of the bladder and urethra by a second row of interrupted sutures were added procedures.

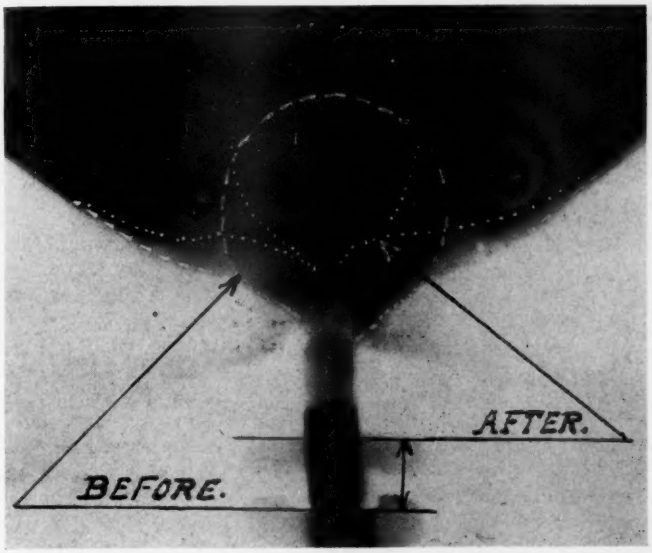


Fig. 10.—Radiograph 9*A*, superimposed on radiograph 9*B*, to show the relative position of the external meatus, the urethra and the bladder, after the Kelly before and after procedure. Before my operation the urethra and bladder have the contour of the "voiding" state during relaxation, but after operation the "relaxing" state is restored during relaxation. This is the requisite for continence.

than before. A urethral radiograph illustrates the result, Fig. 9, *A*. The operation after the method which I described was then done, after which she obtained normal continence. A second radiograph, Fig. 9, *B*, illustrates the end result. Superimposed radiographs before and after operation (Fig. 10) correspond identically with radiographs (Fig. 2) of the normal urethra while relaxing and voiding. The first operation showed no restoration of the urethra but the second operation restored it into the pelvis so that the sphincter mechanism appears normal.

CASE 5.—Let us analyze one more case first reported by my technique in a previous article. This patient, whose operation was a complete failure, was a multiparous woman with prolapse accompanied by a large cystocele, a moderate rectocele, and incontinence for a number of years. She was operated upon in November, 1936. At operation, the bladder and urethra had to be removed from the right ramus by sharp dissection, and in so doing, the bladder was entered just to the right of the trigone. This was immediately closed; then my operation for incontinence was completed. Infection set in between the anterior vaginal wall and the bladder. The anterior wall broke down and on the tenth postoperative day (a retention catheter still being in the bladder) the bed became continuously wet and so persisted for five days, after which the bed was dry. The fistula, fortunately, healed spontaneously and remained so until she went home. She returned two days later, being continuously wet. Intravenous indigo carmine was watched for in the vagina but none appeared while plenty escaped from the urethra. The plicated urethra and bladder had slipped. The infection had produced a solution of the sutures and the urethra partly took on its original contour, Fig. 8, *B*. There was a unilateral failure of maintenance following restoration. The result was a complete failure. During the next year some improvement was obtained by treatment. Cystoscopic examination was done; the ureteral orifices were normal, there were a mild posterior urethritis and a moderate depression of the trigone. In February, 1938, fifteen months after the first operation, she was reoperated upon, repeating the first operation. The end result was better, the patient could be dry from one-half to three hours at a time. Cystoscopic examination revealed the ureteral orifices normal, the right side of the trigone normal, a mild posterior urethritis and a red raised mound about 2 cm. in diameter situated between the internal meatus and the left ureteral orifice. Attached to the base of this was a dense band about ½ cm. in diameter which was attached to the left ramus. Vaginal traction on the band revealed distortion of the trigone laterally, when viewed through a cystoscope. The right side of the trigone was now normal but the left side was tethered to the ramus by an adhesion. I studied my failures and found that some degree of infection between the anterior vaginal wall and the bladder and urethra was the apparent cause. This infection, rapidly dissolving the plicating sutures, permitted all or part of the urethra to resume its original position and adhere again. Doubtless, the seat of this infection was the serum in either paravesical space or between the bladder and urethra and the vaginal wall. To avoid this would probably mean fewer or no infections, and if the hypothesis were right, then more or all successes would follow. How was this to be done? Since the anterior vaginal wall of the vestibule is in intimate contact with the urethra, would it be possible to allow the vagina to granulate under the urethra? The most complete way would be to leave each paravesical space open into the vagina, to leave the plicated urethral wall wide open to agglutinate quickly and wait for the vaginal mucosa to granulate over the lower surface of the urethra and bladder. Eleven months after the second operation (in January, 1939) the patient was reoperated upon. The urethra and bladder were again completely separated from the ramus, the band between the left trigone and the ramus removed. The urethra and bladder walls were plicated and replicated. The vaginal flaps were turned back into the paravesical spaces and lightly held there by packing. The patient had an uneventful convalescence. The vaginal mucosa grew over the lower surface of the bladder and urethra to re-line the vestibule. The patient was allowed to go home on the twenty-sixth postoperative day, having complete control of the urine. Last week, sixteen months after her third operation, she was seen in the follow-up clinic and she stated she can go eight hours without voiding and now never loses a drop of urine.

From this case the following observations are made:

1. Adhesions formed after each of the first two operations must be attributed to something happening which let the urethra and bladder as a whole, or in part, resume its original damaged position and again adhere to the ramus or the vaginal wall.

2. It was most probable that adhesions following the first operation were the result of the infection which caused the break-down of the vaginal wall.

3. It was most probable that the band of scar tissue following the second operation was due to the reorganization of a simple or an infected hematoma which formed between the trigone and the ramus.

4. Since the urethra after the third operation remained in place and was continent without any floor on which to rest during the time the vaginal roof of the vestibule was filling in with granulations, the logical deductions would be (a) that freeing the urethra, then plicating and replicating the urethral and bladder walls is sufficient to replace it to the position of the normal "relaxing" urethra; and (b) that the replacing of the urethra in this manner enables the intrinsic sphincter mechanism to function normally; and (c) the anterior vaginal wall beneath the bladder and the urethra (as far as the urinary tract is concerned) is simply a protective floor on which the bladder and urethra are supported.

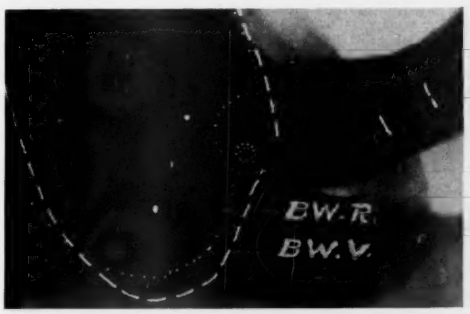


Fig. 11.—Radiograph after my operation on a bladder and urethra, in the "voiding" state (*B.W.V.*) superimposed upon the same bladder and urethra in the "relaxing" state (*B.W.R.*). The "voiding" state is almost identical with the "relaxing" state. The nearer the "voiding" state approaches the "relaxing" state, the more efficient the continence will be.

Now it seems rather drastic to leave the dissected flap of the vaginal wall separate from its opposite mate, so I have for some time been using the Y drain of rubber tissue, one end placed in each paravesical space, as used by Dr. G. G. Ward in his cystopexy operation, and obtaining satisfactory results.

You may well ask, does this operation do what I claim for it? One patient, twice operated on by me, using the Kelly operation, had two successive failures. The third operation 5½ years ago by my method was successful and is satisfactory to this time. Fig. 11 (lateral views) taken over seven weeks after the successful operation shows that, both in the "relaxing" and the "voiding" state, her urethra quite meets the requirement of the normal urethra.

CONCLUSIONS

1. The normal urethra in its "voiding" state is pushed down with the vaginal wall into the vagina, its external meatus is pushed endwise out of the pelvis by varying distances up to 1 cm., and the sphincter muscle surrounding the inner third of the urethra dilates.

2. A varying degree of the "voiding" state (which becomes permanent following relaxation or injury) is present when there is persistent incontinence; the greater the degree the greater the incontinence.

3. When there is no permanent dilatation of the inner third of the sphincter, the urethra may undergo excessive degrees of motion without any incontinence. However, persistent displacement may in time permanently overstretch the inner third of the sphincter, when incontinence will develop.

4. The sphincter mechanism functions with its greatest efficiency when its greatest length is restored, when it is restored as far as possible within the pelvis and restored as high as possible above the vagina.

5. To fulfill the restoration of the urethra it is first necessary to completely separate the urethra from all attachments to the vaginal wall and the rami, both of which, following injury, will hamper the function of the sphincter mechanism.

6. After compeltely freeing the urethra, restoration of the sphincter mechanism can be satisfactorily accomplished by plicating and replicating the under surface of the bladder and urethra.

7. The sphincter mechanism, unhampered by any lateral tractive forces after restoration, will perform its normal function.

8. The sphincter mechanism probably requires no assistance of the levator muscle fibers, and the vaginal wall beneath the bladder and urethra is only a protective floor on which the bladder and urethra lie.

9. Any factor such as infection or hematoma beneath the restored urethra may dissolve the plicating sutures and allow the urethra in whole or in part to resume some degree of the "voiding" state, thereby producing a failure, and re-operation will be necessary. For success, restoration must be bilaterally maintained. Maintained restoration can best be accomplished by very free drainage of the paravesical spaces and open vaginal wall flaps.

10. The success of any incontinence operation will be measured by the fulfillment of the restoration herein described and the maintenance of that restoration.

I wish to thank Dr. A. H. Aldridge, Chief Surgeon of the Woman's Hospital, and Drs. George F. Hoch, Inglis F. Frost, Arthur J. Murphy, and Daniel Mishell for their assistance and interest in this work; Dr. Harriet Mc Intosh for her x-ray contributions and Dr. Joshua W. Davies for his anatomic interest in the problem.

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930 Park Avenue

ARE ESTROGENS CARCINOGENIC IN THE HUMAN FEMALE?*

The Effect of Long-Continued Estrogen Administration Upon the Uterine and Vaginal Mucosa of the Human Female

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THE experimental production of genital and breast carcinoma in rodents and mice by means of estrogens has raised the very important question as to whether there might not be some danger of inducing carcinomas in human beings by the therapeutic administration of estrogens. In the normal female, the genital tract undergoes periods of growth and proliferation followed by periods of regression and rest. This is most strikingly illustrated in the cyclical morphologic changes of the endometrium. Menstruation is followed by a gradually increasing tempo of growth of the endometrium, culminating in the shedding associated with menstruation. These recurring phenomena are dependent upon the cyclic production of adequate amounts of estrogenic hormone by the ovaries. In the human female, furthermore, cessation of ovarian activity is followed by a discontinuation of the cyclical proliferative phenomena in the endometrium and by an advancing regression and atrophy in the endometrium and vaginal mucosa. It is significant, however, that regardless of how atrophic the endometrium or vaginal mucosa may appear microscopically, these structures can be stimulated, by the administration of adequate amounts of estrogenic hormone, to regenerate to a state very similar to that which obtains in women with functioning ovaries. The advanced ageing of the individual apparently does not interfere with the capacity of the epithelial elements of the genital tract to respond in a physiologic manner to estrogens. We have, therefore, available in the estrogens, a group of substances that are powerful growth stimulators and that are capable of inducing intense proliferative activity in the vaginal and uterine mucosa as late as forty years after the cessation of normal ovarian function. In previous communications[1, 2] we have reported our failure to find any evidence of abnormal proliferation in the genital tract of women following estrogen therapy. Because of the widespread therapeutic use of estrogens, particularly in women who fall into the age group in which carcinoma has its highest incidence, we felt it important to submit this problem to further study to determine whether the prolonged administration of estrogens may not result in excessive or abnormal endometrial or vaginal epithelial proliferation, leading possibly to neoplasia.

*Presented before the Third International Cancer Congress, Atlantic City, N. J., September 13, 1939.

MATERIAL

Our studies were conducted on a series of 206 women who have been treated with estrogens over periods varying from six months to five and one-half years and in whom vaginal and endometrial biopsies were performed during varying stages of the period of treatment.

The ages of the patients varied from 25 to 80 years, the majority being over 40 years of age. The patients were being treated for menopausal symptoms, functional amenorrhea, senile vaginitis, and kraurosis vulvae.

The estrogens were administered intramuscularly, in solution in oil (estradiol benzoate, progynon-B*; estradiol dipropionate, di-ovocylin†), by mouth (estradiol, progynon-DH*), by vaginal suppositories (estradiol), by inunction (estradiol) and, during the past year, by implantation of pellets and crystals (estradiol, estradiol benzoate, and estradiol dipropionate). The hormones were administered in individual doses varying from 10,000 I.U. to 150,000 I.U. The total amount given varied from 500,000 I.U. to 23,400,000 I.U.

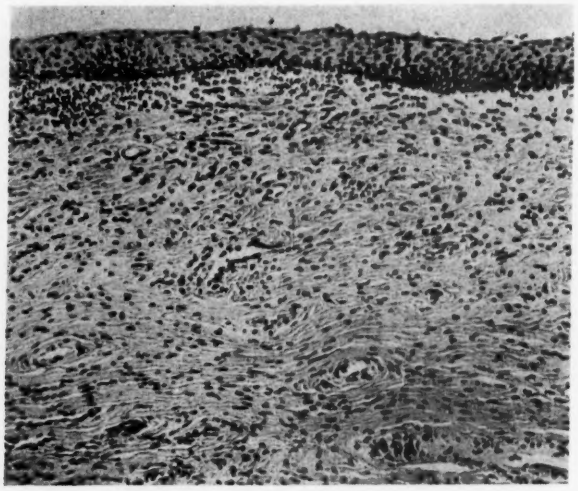

Fig. 1.—Case E. V., aged 52 years, spontaneous cessation of menstruation four years previously. Atrophic vaginal mucosa before treatment, indicating estrogen deficiency.

RESULTS

Effect of Estrogens Upon the Atrophic Mucosa.—The first noticeable effect of estrogen therapy upon the atrophic vaginal mucosa is a rapid proliferation of the basilar epithelial cells. This is discernible as early as four days after the intramuscular administration of as little as 100,000 I.U. (total) of estrogens. Proliferation proceeds at a rapid pace, leading to an increase in the number of epithelial layers and resulting in desquamation of some of the superficial epithelial cells. The proliferative activity is, however, not uniform, areas of hypoplasia being found adjacent to areas of active proliferation. This explains the finding of large, squamous, epithelial cells scattered among the atrophic cells

*For the estradiol benzoate (progynon-B) and estradiol (progynon-DH) used in this investigation, we are indebted to Dr. Erwin Schwenk, of the Schering Corporation, Bloomfield, N. J.

†For the estradiol dipropionate (di-ovocylin), we are indebted to Mr. Robert C. Mautner, of Ciba Pharmaceutical Products, Summit, N. J.

in the vaginal smears taken at this stage. If the estrogen administration is continued, there is a progressive increase in the number of epithelial layers, accompanied by an active process of desquamation. The latter is manifested by the appearance of a thick, white, vaginal secretion which consists almost entirely of desquamated, large, squamous, epithelial

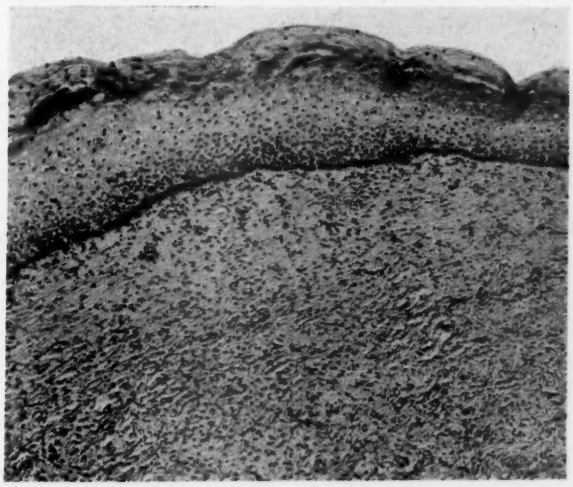

Fig. 2.—Vaginal mucosa showing incomplete regeneration after 600,000 I.U. of estradiol benzoate given during two weeks.

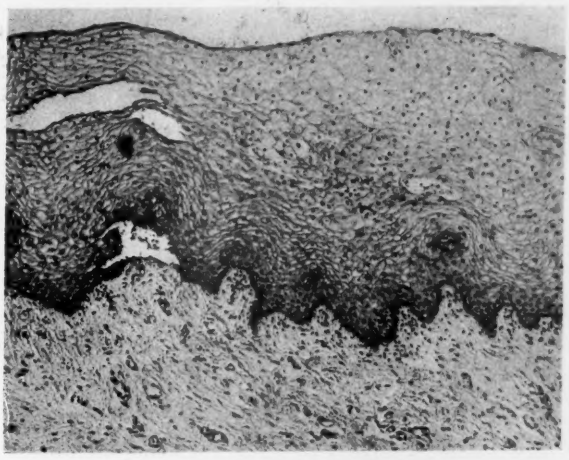

Fig. 3.—Vaginal biopsy nine weeks later (after 2,870,000 I.U. of estradiol benzoate) showing advanced proliferation.

cells. This degree of proliferation is attained with doses varying from 200,000 to 2,000,000 I.U. of estradiol benzoate administered intramuscularly. There is an amazingly wide variation in the individual response to equal amounts of the hormone. This variation in the proliferative response is probably due to a combination of factors, viz., the degree and duration of estrogen deprivation prior to the institution of estrogen

therapy, the rate of absorption, and the rate of excretion of the hormone. In some cases, doses of more than 2,000,000 I.U. failed to induce complete morphologic restitution. It is interesting to note that once morphologic restitution has been attained further increase in the dosage does not appear to produce any further progress in the proliferative response. Actually, in a number of cases, the vaginal mucosa appeared to be less

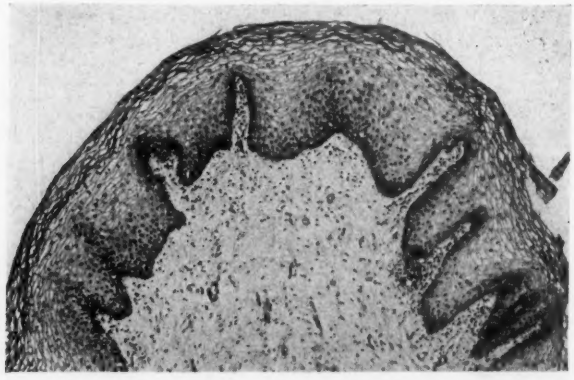

Fig. 4.—Vaginal biopsy after 20,200,000 I.U. of estradiol benzoate. Note absence of excessive or abnormal epithelial proliferation.

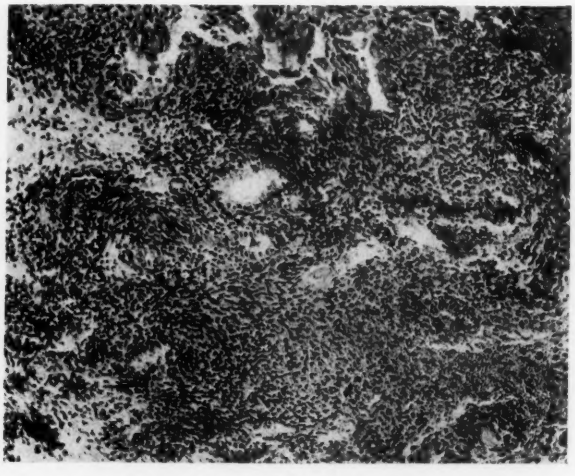

Fig. 5.—Case E. V.; preliminary endometrial biopsy showing atrophy of the endometrium, indicative of estrogen deficiency.

regenerated after the patient had received the larger doses than after the smaller ones. Compare Fig. 3 (showing vaginal mucous membrane after 2,870,000 I.U. of estradiol benzoate) with Fig. 4 (biopsy taken from the same patient after a total of 20,200,000 I.U. of the hormone was given). It is extremely significant that continuing the estrogen administration to this enormous dose did not produce any signs indicating excessive or abnormal proliferation.

Effect of Estrogens on the Endometrium.—The atrophic endometrium (Fig. 5) responds more slowly than the vaginal mucosa to estrogen stimulation. Not infrequently, amounts of estrogens (400,000 to 600,000 I.U.) that produce striking epithelial growth in the vaginal mucosa will result in only slight proliferation in scattered areas in the endometrium. As

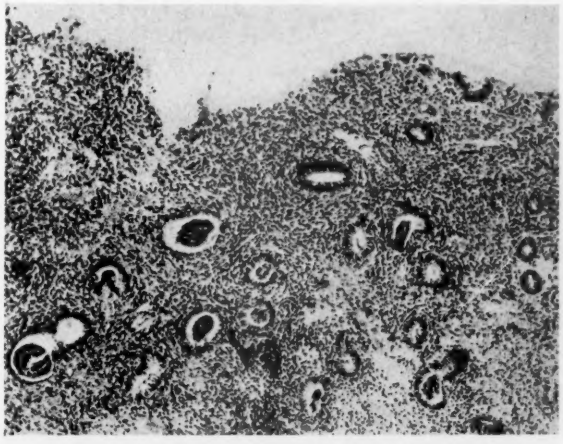

Fig. 6.—Endometrium after total of 1,200,000 I.U. of estradiol benzoate in four weeks, revealing proliferative pattern.

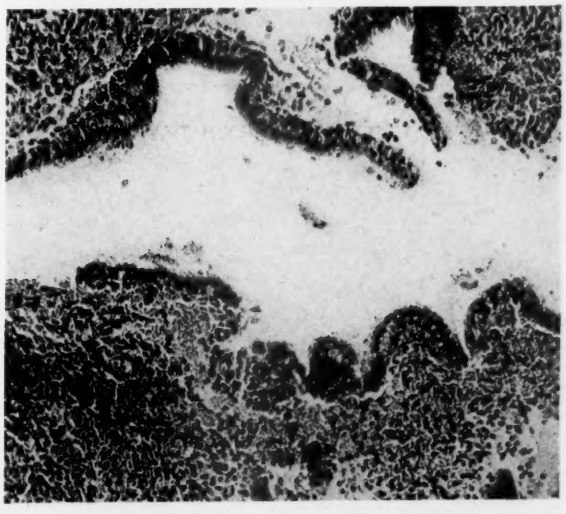

Fig. 7.—Endometrial biopsy taken during period of estrogen-induced bleeding. Patient had been bleeding for three days when this biopsy was obtained. Total dosage at this time was 1,500,000 I.U. of estradiol benzoate. Bleeding continued for four more days. Estrogens were not administered during the period of bleeding.

the dosage is increased, approaching the 1,000,000 I.U. level, the endometrium shows a more definite and more uniform proliferative response, resembling the normal proliferative pattern found in the normal postmenstrual phase of the cycle (Fig. 6). Uterine bleeding usually occurs after the patient has received approximately 1,000,000 to 1,500,000 I.U.

during four to six weeks. At this stage the endometrium is found to exhibit signs of active proliferation with some evidence of gland distention. Examination of the uterine blood in several cases has revealed

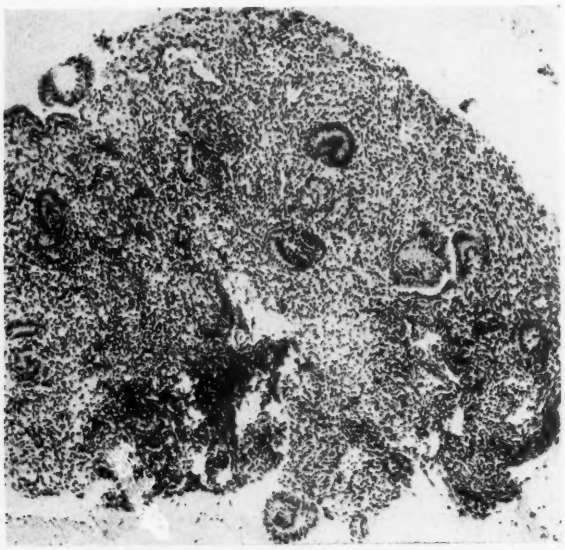

Fig. 8.—Endometrial biopsy taken four days after cessation of estrogen-induced bleeding and before the re-instatement of estrogen therapy. The biopsy reveals the endometrium to have regressed to a state of inactivity resembling the pre-treatment status.

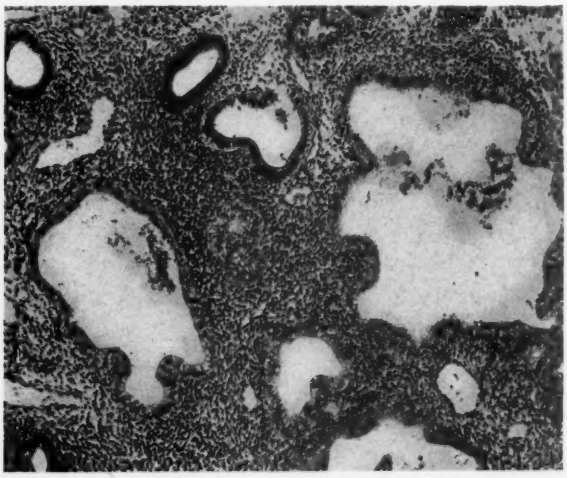

Fig. 9.—Case H. S., aged 55 years, menopause five years previously. Endometrial biopsy after a total of 18,500,000 I.U. of estradiol benzoate, administered during a period of thirty-four months. The endometrium is in a state of active proliferation with some cystic glandular dilatation. Estrogens were then stopped; uterine bleeding began six days later and lasted for five days.

desquamated fragments of endometrium containing glands and stromal cells. Biopsies performed during the period of bleeding exhibited various stages of proliferation associated with distended (cystic) glands.

Biopsies performed after the cessation of bleeding usually revealed a *quiescent* and, in many cases, an *atrophic endometrium*. Continued administration of estrogens after the uterine bleeding had ceased resulted in a repetition of the same proliferative process, followed by desquamation and bleeding and a return of the endometrium to its quiescent state. In some cases, this cyclical bleeding occurred at intervals of four to ten weeks for many months (six to thirty-eight months). It is noteworthy that in these cases the endometrium at the end of these long periods of estrogen stimulation, punctuated by recurrent episodes of bleeding, does not reveal any greater proliferative activity than after the initial course of estrogen stimulation.

Similar morphologic studies performed with estradiol dipropionate administered intramuscularly, estradiol administered orally, by skin inunctions, and by vaginal suppositories revealed essentially similar results.

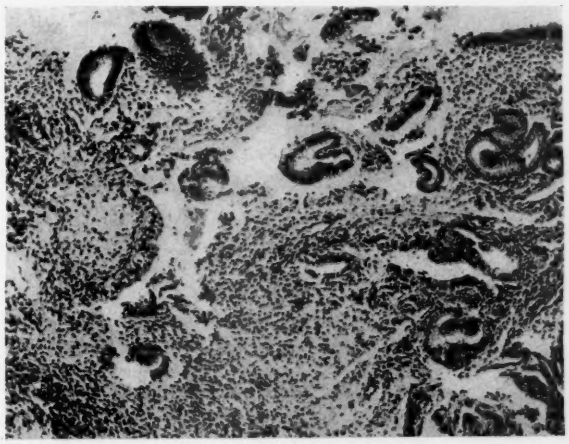

Fig. 10.—Endometrial biopsy taken ten days after the termination of the bleeding episode. The endometrium is in a quiescent, almost atrophic, state.

SUMMARY AND CONCLUSIONS

1. The administration of estrogens to women suffering from an estrogen deficiency results in regenerative changes in both the vaginal and uterine mucosa.

2. If estrogens are administered continuously, in adequate therapeutic doses, the vaginal mucosa responds with an orderly progressive regeneration of the epithelial layers, resembling the histologic pattern of the adult cyclical female with normal estrogen production.

3. Continued administration of estrogens leads to increased desquamation of the superficial epithelial layers without producing any signs of excessive or abnormal epithelial proliferation.

4. The atrophic endometrium responds to adequate estrogen therapy with an orderly regeneration of the epithelial, glandular, and stromal elements. Continued administration of estrogens (at the rate of approximately 1,500,000 I.U. per month) usually results in the appearance

of cystic glands, in some cases resembling the Swiss cheese pattern, associated with active proliferation of the stroma. In no case was any evidence of abnormal proliferation noted.

5. The same process of endometrial growth, desquamation (associated with bleeding) and regression, followed by regeneration, can be reproduced cyclically by repeating the course of estrogens.

6. It is obviously impossible in human beings to administer the huge doses of estrogens over the long periods of time that would justify comparison with the experimental production of carcinoma in rodents. However, the conclusion seems warranted, on the basis of these studies that, within the limits of the dosage used in this investigation (up to 53,400,000 I.U.), there appears no evidence to justify the fear that carcinoma of the genital tract may result from the therapeutic use of estrogens.

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THE PULSE AND RESPIRATORY VARIATIONS IN NORMAL WOMEN DURING LABOR*

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SINCE it has been suggested that the variations of the pulse and respiratory rate during labor would afford a warning of the approach of serious cardiac insufficiency in patients with heart disease,[1] it seemed important to determine the character of the variations in normal women. Such studies have not been found in the literature although recent work has touched upon many other phases of the cardiorespiratory reactions of pregnancy and labor. This recent work has been in relation to the prelabor period. Few investigations have been concerned with labor itself.

Martin[2] found that the pulse increased with the pains and returned to normal between pains during early labor but later, when the pains became more severe, he found that the pulse remained elevated. Probyn-Williams, and Cutler[3] found the average pulse rate during labor to be 89. Gewurz[4] noted a lability of the pulse during labor with stability during the puerperium. He also observed an increase of the pulse rate during labor with gradual decline in the puerperium. Hamilton[5] stated that from the time the patient enters the hospital until she is delivered and is returned to her room, the pulse rate should be 100 or less, and any elevation over that value is due to insult: either medical, surgical, or obstetric.

The subject of post-partum bradycardia has received considerable attention, particularly during the second half of the last century. Its

*Read at a meeting of the Section on Obstetrics and Gynecology, New York Academy of Medicine, December 17, 1940.

existence has been denied by some authors while others found it in 90 per cent of the patients. The majority reported an incidence greater than 20 per cent. The onset of the bradycardia is reported variously at from two hours to nine days post partum, and its duration at from several days to several weeks. Multiparas are said to show more slowing of the pulse than primiparas. Few authors have compared figures on the same patients before and after delivery. Heart block might be suspected from some of the extremely low rates reported, for they are in the zone that would suggest this condition.

Respirations were noted by Gewurz[4] to be usually normal during labor and followed by a respiratory arrhythmia with onset shortly after delivery, and lasting for about nine days.

The present study was undertaken in an attempt to establish the normal behavior of the pulse and respirations during labor, and to evaluate, if possible, the influence of such related factors as total duration of labor, duration of the second stage, and analgesia. A similar study in cardiac patients is under way.

Although no definite routine of analgesia is followed in the New York Lying-in Hospital, the following may be given as the most common sequence.

In early labor if the pains are not unduly troublesome, analgesia is delayed until the cervix is found to be 4 or 5 cm. dilated, and the pains become more severe. At this time morphine and scopolamine are administered (morphine 0.010 Gm. and scopolamine 0.0004 Gm.). If labor progresses satisfactorily no further analgesia may be used. Occasionally, if pains are very severe and delivery seems reasonably remote, another dose of morphine may be given, or when the cervix reaches 7 cm. dilatation, rectal instillation of an ether, oil, and quinine mixture is given (75 c.c. ether, 2.6 c.c. alcohol, and 0.6, or 1.2 Gm. of quinine). In not a few instances, particularly in patients entering the hospital late in labor without having suffered unduly, no analgesia may be used, or possibly only rectal instillation of the mixture described above. After full cervical dilatation, patients receive nitrous oxide and oxygen during contractions and bearing down is encouraged until sufficient amount of the presenting part is visible to permit delivery. At this time ether is added to the mixture of gases.

RESULTS

One hundred and eighty patients were studied: 153 primiparas and 27 multiparas. The pulse and respirations were recorded by graduate nurses every fifteen minutes from the time of admission in labor until delivery, and thereafter on the wards every four hours. A chart was made of each case similar to those of Figs. 1 to 5 and from a study of these charts the following data were obtained. It was found unsatisfactory for the purposes of summary to consider each separate pulse and respiratory count because certain figures were only reached once or twice, and the differences between successive counts were often considerable and at times alternately up and down as shown by the pulse counts in the central portion of Fig. 5. For this reason each chart was summarized by considering the average level of the pulse and respirations for 3 or 4 successive counts, the pulse level being considered to the nearest multiple of 10 and the respiratory level to the nearest even number. Isolated aberrant counts were disregarded such as the two respiratory counts of 38 seen in Fig. 5. This chart was summarized as the pulse reaching 140 and the respirations 28 per minute. Of the 180 patients studied, only 10 (5 per cent) showed an increase in pulse rate of more than 20 per minute. Of the remaining 170 patients, 87, or about half, failed to show any change in the pulse during

labor. Of the total patients studied, 17 (9 per cent) showed an increase in respirations of more than 8 per minute. Of the remaining 163 patients, 75, or slightly less than one-half, showed no change in respirations during the course of labor. Fifty-six patients (31 per cent) showed no change in either pulse or respirations during labor.

Because some patients appeared first with a slightly elevated pulse, such as 85 or 90, it seemed better to consider the maximum pulse rate and respiratory rate which was reached and maintained for the duration of three consecutive counts. On this basis it was found that in 41 patients (23 per cent) the pulse rose to above 110 or the respirations to above 24 per minute. In 18 patients (10 per cent) the pulse rose above 110 per minute, and in 34 patients (19 per cent) the respirations rose above 24 per minute. There were 12 patients (7 per cent) having both the maximum pulse above 110 and respirations above 24 per minute. All of the 10 patients with pulse increasing more than 20 per minute were in the group with pulse rising above 110 or respirations above 24 per minute. Fifteen of the 17 patients with respirations increasing more than 8 per minute fell in the same groups.

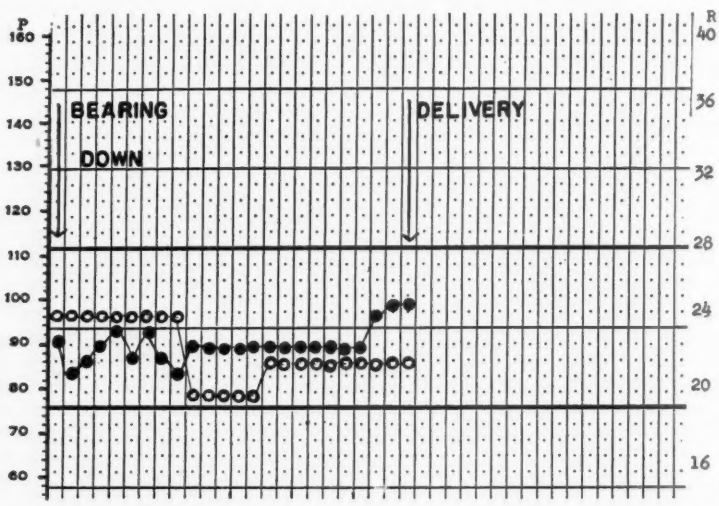

Fig. 1.—Pulse and respirations in the latter part of labor. Primigravida. Total labor 81 hours. Recordings every 15 minutes. Practically no change in pulse or respirations throughout entire labor. ○ respirations; ● pulse.

Of the patients with the pulse rising above 110: 7 reached 120 (respiration counts from 24 to 28); 7 reached 130 (respiration counts from 20 to 40); and 4 reached 140 (respiration counts of from 28 to 32). Of the patients with respirations rising above 24 per minute: 2 reached 26 (pulse counts of 90); 12 reached 28 (pulse counts from 80 to 140); 4 reached 30 (pulse counts from 80 to 140); 12 reached 32 (pulse counts from 90 to 140); and 4 reached 40 (pulse counts from 80 to 130). Neither intrapartum lability of pulse, nor post-partum bradycardia, nor post-partum respiratory arrhythmia was observed.

Table I illustrates graphically certain of the above features, while Table II shows the frequency of the various combinations of different degrees of pulse and respiratory disturbance. Figs. 1 to 5 are copies of actual charts illustrating certain frequent types of reaction. Fig. 1 shows the chart of the last six hours of a long labor. The respirations were 24 per minute at first but later fell to 20 after the administration of morphine and then rose to 22 at the end. Fig. 2 shows the chart of the last nine hours of a twenty-seven-hour labor. The pulse remained in the neighborhood of 80 for most of the time but at the end rose to 84. The respirations remained at 18 until the second stage when they rose gradually to 22. Fig. 3 is the chart of the last 5.5 hours of a 16.5 hour labor. During the earlier

part of the labor the pulse remained at about 80 and the respirations at 22. The pulse rose to 84 and 86 just before the second stage and the respirations remained at 20 only to suddenly rise to 39 at the onset of the second stage. Reactions of this sort are relatively uncommon, occurring in only 8 cases of the series (4.5 per cent) and generally are observed in women of a nervous or neurotic type. Fig. 4 shows the last seven and one-half hours of a twenty-five-hour labor. The pulse had remained at about 90 and the respirations at 20 before this portion of the chart was reached. At about the beginning of the second stage the pulse rose to about 120 at which level it remained and the respirations rose more gradually to a maximum of 24 and then gradually fell to 22. This is a moderately severe reaction which had it been observed in a cardiac patient might have occasioned some alarm. Fig. 5 is a record of the last nine hours of a fifty-two-hour labor. Previous to this

TABLE I. BEHAVIOR OF PULSE AND RESPIRATIONS DURING LABOR IN 180 NORMAL WOMEN

Cases	*Pulse*		
4 reached 140 (resp.: 28, 28, 30, 32)			
7 reached 130 (resp.: 20, 24, 28, 32, 36, 40, 40)			
7 reached 120 (resp.: 24, 24, 24, 24, 24, 24, 28)			
Pulse over 110 per minute 18, or 10%			
Pulse unchanged 87, or 51%		No change either pulse or resp. 56 or 31%	Pulse over 110 and resp. over 24 12 or 7%
Respirations unchanged 75, or 42%			
Respirations over 24 per minute 34, or 19%			

Cases	*Resp.*
2 reached 26 (pulse:	90, 90)
12 reached 28 (pulse:	80, 80, 94, 100, 100, 100, 100, 110, 120, 130, 140, 140)
4 reached 30 (pulse:	80, 90, 130, 140)
12 reached 32 (pulse:	90, 90, 90, 90, 90, 90, 90, 90, 100, 110, 130, 140)
4 reached 40 (pulse:	80, 100, 130, 130)

In the upper section of this table is given the maximum respiratory rate of each individual with a pulse over 110. The number of patients with a pulse of 120, 130, and 140 is indicated, and the respiratory rates in the individual patients of each group. Similarly the lower section shows the patients with maximum respiratory rates over 24 and the maximum pulse rates in the individual patients of each grade of respiratory increase.

TABLE II. THE PERCENTAGE DISTRIBUTION OF VARIOUS TYPES OF PULSE AND RESPIRATORY REACTIONS

No change in either pulse or respiratory rates (56 cases)	31%
Mild reactions:	
No change in pulse rate, respiratory rate increased but did not exceed 24 (2 cases)	1%
No change in respiratory rate, pulse rate increased but did not exceed 110 (2 cases)	1%
Moderate reactions:	
Pulse and respiratory rates both increased but pulse rate did not exceed 110, nor respiratory rate exceed 24 (76 cases)	43%
No change in pulse rate, respiratory rate exceeded 24 (24 cases)	13%
No change in respiratory rate, pulse rate exceeded 110 (20 cases)	4%
Marked reactions:	
Pulse rate exceeded 110 and respiratory rate exceeded 24 (12 cases)	7%

portion of the chart the pulse had been fairly level at about 100 and the respirations at 20. Two and one-half hours before the second stage the pulse began to rise, eventually reaching 120 but the respirations remained at 20 until the bearing down began, when the pulse promptly rose to 140 and the respirations to 28. These

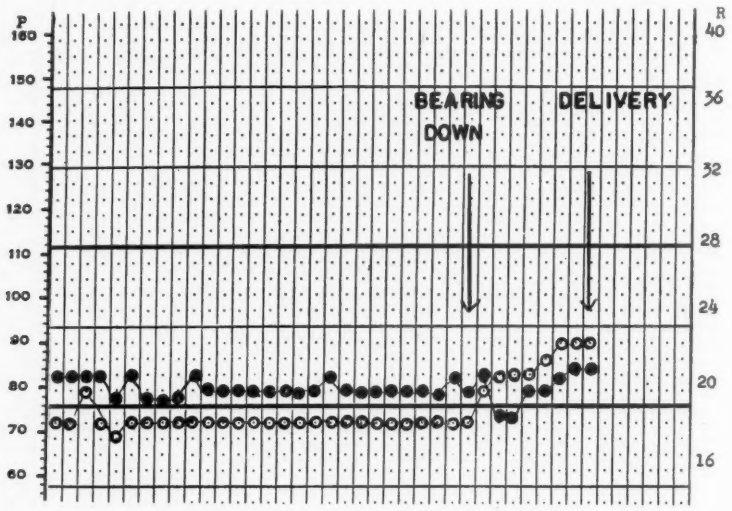

Fig. 2.—Pulse and respirations in the latter part of labor. Primigravida. Total labor 27½ hours. Recordings every 15 minutes. Small increase in respiratory rate and no change in pulse rate, pulse having remained at 80 and respirations at 18 throughout earlier part of labor. ○ respirations; ● pulse.

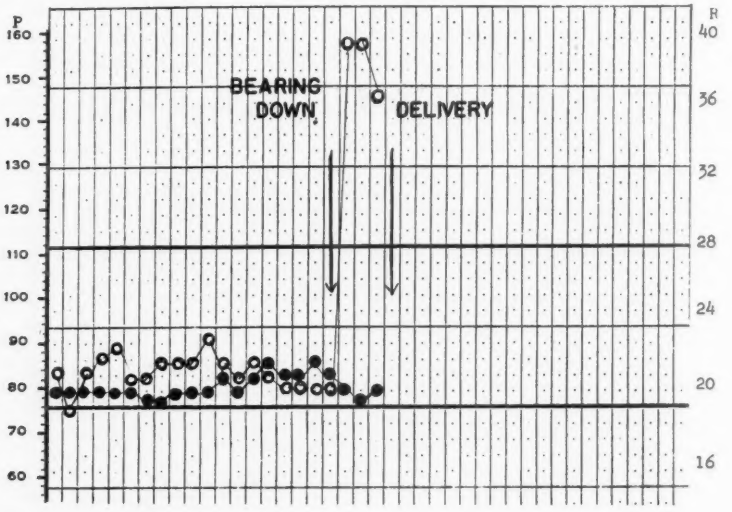

Fig. 3.—Pulse and respirations in the latter part of labor. Multigravida. Total labor 16½ hours. Recordings every 15 minutes. Large increase in respiratory rate without change in pulse rate, pulse having remained at 80 and respirations at 22 throughout earlier part of labor. ○ respirations; ● pulse.

levels were approximately maintained for three hours until delivery, after which the pulse and respirations fell to normal levels in eight hours. Had this picture appeared in a cardiac patient it would so strongly have suggested cardiac strain that in all probability labor would have been accelerated by appropriate means. It is of greatest importance to appreciate that such severe cardiorespiratory reactions may

appear in healthy women and noteworthy that they appeared only during the second stage.

In order to find some explanation of this phenomenon which appears in 7 per cent of our patients, we have considered various possibilities. Anemia can be

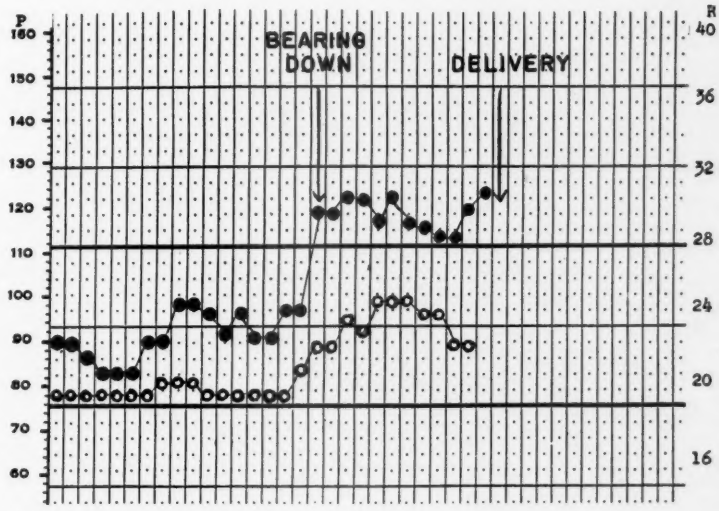

Fig. 4.—Pulse and respirations in the latter part of labor. Primigravida. Total labor 25 hours. Recordings every 15 minutes. Small increase in respiratory rate and large increase in pulse rate, pulse having remained at 90 and respirations at 20 throughout earlier part of labor. ○ respirations; ● pulse.

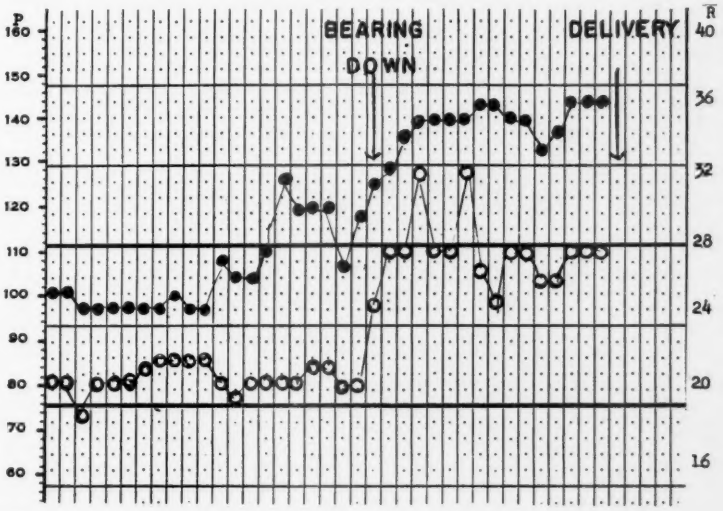

Fig. 5.—Pulse and respirations in the latter part of labor. Primigravida. Total labor 52 hours. Recordings every 15 minutes. Graph showing terminal increase in pulse and respiratory rates, pulse having been at 100 and respirations at 20 throughout earlier part of labor. ○ respirations; ● pulse.

ruled out, as none of the patients in this group was anemic nor had any other medical complication. It was observed that during labor pains there was usually a slight increase of pulse rate and a slight decrease of respiratory rate. When the contractions had subsided there was a return to the former levels. It was observed also as can be seen in the figures that when a persistent increase of pulse or respira-

tions was present, it almost always began with the second stage of labor or shortly before.

To determine whether these pulse and respiratory changes might have been affected by analgesia or by the total duration of labor or by the duration of the second stage, an analysis was made as shown in Table III.

Because of the possibility that some of the pulse and respiration values may have been influenced by drugs, it is worth while to consider briefly the action of such drugs as the patient may have received.

Morphine is a central respiratory depressant. By virtue of its action on the vagus nerve it also causes slowing of the heart. Pain is an antidote for morphine, however, and can in part nullify its effects. Scopolamine paralyzes the vagal endings and accordingly tends to counteract the effects of morphine. Rectal ether initially tends to produce respiratory irregularity. Ultimately the respirations are slowed and become regular. When a combination of the above drugs is used, their varied

TABLE III

Pulse Rising Over 110 or Respirations Rising Over 24

	EITHER		PULSE		RESPIRATIONS		BOTH	
	PATIENTS	%	PATIENTS	%	PATIENTS	%	PATIENTS	%
	41	23	18	10	34	19	12	7
Analgesia								
62 none*	15	24	7	11	13	21	4	6
32 ms, re	8	25	3	10	7	22	3	10
42 ms	7	17	4	10	8	21	3	7
29 re	11	37	4	13	6	21	2	6
Total labor over 30 hr. 46 patients 26%	18	39	8	17	15	33	5	11
Total labor 30 hr. or less 134 patients 74%	23	17	10	7	20	14	7	5
Second stage over 2 hr. 56 patients 31%	14	25	5	8	14	25	5	9
Second stage 2 hr. or less 124 patients 69%	27	21	13	10	21	16	7	6

No Change in Pulse or Respirations

	BOTH		PULSE		RESPIRATIONS	
	PATIENTS	%	PATIENTS	%	PATIENTS	%
	56	31	87	51	75	42
Analgesia						
62 none*	23	37	33	53	30	48
32 ms, re	11	34	17	53	12	37
42 ms	13	30	22	52	19	45
29 re	9	31	15	51	14	48
Total labor over 30 hr.	10	21	18	38	14	30
Total labor 30 hr. or less	46	34	69	51	61	45
Second stage over 2 hr.	10	18	15	26	11	19
Second stage 2 hr. or less	46	37	72	58	64	51

*None, no analgesia; ms, morphine and scopolamine; re, rectal ether.

actions scarcely allow one to predict the net result upon pulse or respirations.

A study of Table III fails to show any correlation between analgesia and pulse or respirations during labor. In comparing the groups which did and did not receive analgesia, one is unable to find a significant difference in the pulse or respiration values. Nor do the values with any one type of analgesia seem to differ from those with any other.

The data of Table III indicate, however, that both an increase in the total duration of labor and also in the duration of the second stage, tend to produce a rise in the pulse and respiration values. This increase generally, as has been said, occurs at the time of the second stage or shortly before. Some patients experience the urge to push with the contractions before full cervical dilatation is reached and actually, if a rise in pulse and respirations is to occur, it starts with the appearance of bearing-down efforts, and the initial rise begins within the first half hour of such effort.

There were, however, several instances of prolonged labor during which the pulse and respirations failed to rise significantly or at all. In all cases of prolonged labor, maternal exhaustion and acidosis were treated by oral and parenteral administration of glucose and fluids, and it is believed that without this type of obstetric care more of these patients might have shown an elevation of pulse and respirations.

It is of interest that 8 of the 18 patients with the pulse rising over 110 showed persistence of tachycardia throughout the puerperium, although there were no instances of anemia, puerperal hemorrhage, infection, thyroid, or cardiorespiratory disease. Post-partum tachycardia was only found in patients who had shown a rise of pulse rate to over 110 during labor. In some patients abdominal, rectal, or vaginal examination was observed to be sufficient to significantly raise the pulse for a short period. This suggests that anxiety might have been the factor in the rapid heart rate of these patients and possibly also in those with persistent post-partum tachycardia. Although post-partum bradycardia was not observed, it would seem reasonable to explain relative slowing of the pulse on the basis of the bed rest incident to the early puerperium.

Only one patient had a respiratory rate over 20 during the first day post partum. She had shown an increased respiratory rate during labor. She was a primipara and had a labor of nineteen hours' total duration, being forty-eight minutes in the second stage. Before the second stage, her pulse had varied from 80 to 90 and her respirations from 22 to 24. About three-quarters of an hour before the second stage her pulse and respirations began to rise gradually and during the second stage her pulse reached 110 and her respirations, 28. The general picture of this woman's chart resembled rather closely that of Fig. 5. The first day post partum her respirations varied from 24 to 22, on the second day they varied from 22 to 20, and thereafter they were 20 or less. The pulse post partum was over 100 once or twice each day for the first 4 or 5 days. No pelvic complication was discovered. There were no pulmonary râles.

CONCLUSIONS

In normal women during labor the pulse and respirations usually change but little until voluntary bearing-down efforts are brought into play. This occurs at or shortly before full dilatation of the cervix. There is a short insignificant increase in the pulse and decrease in the respirations during contractions with return to former levels during the intervals.

With the onset of bearing-down efforts the pulse, or respirations, or both may remain unchanged or may increase. The pulse seldom increases more than 20 beats per minute but exceeds 110 per minute in 10 per cent of the cases. Respirations seldom increase more than 8 per minute but exceed 24 per minute in 19 per cent of the cases. It is unusual for both pulse and respirations to exceed these values, this occurring in only 7 per cent of the cases.

No correlation could be found between the level of pulse or respirations and either the use of analgesia or the particular analgesic used.

Prolonged labor and prolonged second stage increase the liability to acceleration of pulse and respirations.

Other than a transient rise during labor pains, lability of pulse during labor was not prominent. Post-partum bradycardia and post-partum respiratory arrhythmia were not observed.

Relative slowing of the pulse post partum is not out of proportion to the bed rest incident to that period.

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RHEUMATIC HEART DISEASE IN PREGNANCY

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PREGNANCY complicated by rheumatic heart disease has been the subject of a recent study at the Margaret Hague Maternity Hospital. A total of 345 cases were reviewed, dating from 1933 to 1939. All cases, private, clinic, and "neglected," were included. By the neglected case we mean to designate the pregnant woman who, without previous medical attention, was first seen by us in cardiac failure. The incidence of heart disease at this hospital for the years studied was 1.2 per cent, based on total admissions. This figure falls within the range reported by kindred institutions in this country. Rheumatic heart disease made up 95 per cent of all cases of heart disease.

By and large it can be said that the treatment of heart disease once present resolves itself into the effort to prevent decompensation. In the pregnant woman with heart disease, the occurrence of heart failure is of vital importance. Because of this self-evident fact every effort should be made to prevent this complication. We feel it possible to foretell fairly accurately which patient will decompensate when burdened with a pregnancy if the deleterious effects of this burden are not counteracted by bed rest. Three extremely important prognostic aids appeared in the analysis of our cases. All three are contained in the patient's history, (1) the functional cardiac capacity prior to pregnancy, (2) the patient's age, and (3) the presence or absence of previous cardiac failure.

We followed the New York Heart Association classification, as follows:

Class 1: Patients with cardiac disease and no limitation of physical activity.
Class 2A: Patients with cardiac disease and slight limitation of physical activity.
Class 2B: Patients with cardiac disease and marked limitation of physical activity.
Class 3: Patients with cardiac disease who are unable to carry on any physical activity without discomfort.

Of 345 patients with rheumatic heart disease seen since 1933, 77 decompensated, an incidence of 22.3 per cent. Table I shows the incidence of cardiac failure in relation to the functional classification.

TABLE I. CARDIAC FAILURE IN RELATION TO FUNCTIONAL CLASSIFICATION

CLASS	TOTAL	FAILED
1	143	4 — 2.8%
2A	116	9 — 7.7%
2B	81	59 — 72.8%
3	5	5 — 100%
	345	77 22.3%

Thus the incidence of failure in pregnancy quite naturally increases as the functional capacity in the nonpregnant state decreases. The burden of pregnancy can be borne without serious difficulty by the comparatively well-functioning hearts, while the same burden will cause decompensation in the badly incapacitated group.

Additional prognostic information is obtained from the age of the patient. We have divided our patients into five-year age groups ranging from fifteen to over forty, and determined the incidence of decompensation in each group (Table II).

TABLE II. CARDIAC FAILURE IN RELATION TO AGE

YEARS	TOTAL	FAILED
Less than 20	32	4 — 12.5%
21-25	135	13 — 9.6%
26-30	100	26 — 26.0%
31-35	49	16 — 32.6%
36-40	25	14 — 56.0%
More than 40	4	4 — 100%
	345	77 22.3%

In general, it may be said that the older the cardiac patient the greater the possibility of a breakdown occurring in the pregnant state. The minor discrepancy shown in the less-than-twenty group is possibly due to the relatively small number in this class. To make the association between age and incidence of decompensation more striking, the patients may be divided into two groups, those less than thirty and those more than thirty years of age. The failure rate in the younger group was 16.1 per cent, compared to 43.6 per cent in the older group. It should be added that the patient's age and the functional capacity of her heart are certainly dependent to some extent upon one another. In our series the older groups very naturally contained the higher percentages of functionally bad hearts.

What a pathologic heart will do when forced to support a pregnancy may to some extent be foretold by its previous record. Did the patient ever decompensate before? In our series there were 11 patients who had decompensated previously but did not compensate in the pregnancy under consideration. Thirty-three patients gave a history of cardiac failure in the past and decompensated again in the pregnant state.

Thus, of 44 women who suffered broken compensation previously, 75 per cent decompensated again when pregnancy complicated the heart disease. If a patient has never decompensated before, her chances of cardiac failure when the burden of pregnancy is assumed are 14.1 per cent.

TABLE III. PROGNOSTIC VALUE OF HISTORY OF DECOMPENSATION

Cardiac failure previously *but not* in this pregnancy	11
Cardiac failure previously *and again* in this pregnancy	33
Cardiac failure for the *first time* in this pregnancy	44
Previous cardiac failures	44
Previous cardiac failures and again in this pregnancy	33 — 75%

A similar association was reported in 1926 by G. H. Hunt.[1] In his series of 156 cases, 50 per cent of the previous cardiac failures decompensated again, as compared to a 17 per cent cardiac failure rate in pregnancy when no decompensation had occurred before. His total failure rate of 21 per cent matches very closely the 22.3 per cent in our group and the 19.2 per cent reported by the Boston Lying-in Hospital.

We feel certain that attention to these prognostic signs has helped us immeasurably in our handling of the pregnant woman with heart disease. In the last 103 consecutive cardiac patients delivered at the Margaret Hague Maternity Hospital (these are not included in the above statistics), there have occurred two failures, one of which was probably preventable, an incidence of less than 2 per cent. This was accomplished by careful prenatal observations at frequent intervals, by the prompt institution of absolute bed-rest at the first suspicion of any decrease in cardiac reserve, and, most important, by the hospitalization of any patient who presented a history of previous cardiac failure or a combination of prognostic signs that indicated the possibility of difficulty. It has been our experience that if the need for bed rest arises at any period in the pregnant state the rest must be absolute and continuous for the duration of the gestation.

Feeling satisfied that by the application of the principles mentioned above we have been able to decrease the decompensation rate among our pregnant women with rheumatic heart disease to an almost negligible incidence, we felt it was important to determine when in the pregnancy the patient might be expected to experience the most difficulty. Knowing at what time the burden of pregnancy exerts its maximum effect upon the heart would enable us to fortify our therapeutic attack with preventive measures. Before presenting the analysis of our patients with this view in mind, it is necessary to note that a fairly clear concept of the dynamics of the circulation of the normal pregnant woman has resulted from the laboratory and clinical work of several observers.[2] Much has been done in studying the circulatory burden in pregnancy, but only a few pertinent determinations will be mentioned here. Studies of the total blood volume have usually shown a progressive increase from the early months of pregnancy to a maximum in the eighth month. During the last month of pregnancy the blood volume decreases, from an average of 45 per cent above the normal

for the nonpregnant woman to reach normal two weeks post partum. Experimentally it has been shown that increased blood volume leads to increased cardiac output. Studies on the velocity of blood flow show a gradual increase during the course of pregnancy and a slowing up as the expected date of confinement approaches. Thus the cardiac load begins to increase when the pregnancy begins and progresses steadily to reach a maximum during the eighth month. In the last month of pregnancy, not at delivery but during a period of four to six weeks preceding it, the blood volume, the cardiac output, and the velocity of blood flow tend to return toward normal levels with a consequent diminution of cardiac work. Through such studies it has been possible to "see" the burden that the pregnancy places upon the heart, a burden carried by the normal heart with no, or at least little, difficulty. However, this seemingly extra load is sufficient to embarrass a previously damaged heart, unless other factors known to strain cardiac capacity are appreciated and strenuous attempts made to remove the "medically removable" burdens. We have attempted to correlate this physiologic concept with clinical experience.

Table IV shows when the failures in our series occurred.

TABLE IV. CARDIAC FAILURE IN PREGNANCY: TIME OF OCCURRENCE

TIME	NO.	PER CENT
1-6 mo.	40	51.9
7-8 mo.	22	28.5
9 mo.	8	10.3
Labor	5	6.4
Puerperium	2	2.5
	77	

Eighty per cent of the cardiac failures in this series were found to occur during the first eight months, with the greatest incidence concentrated in the seventh and eighth months. Thus, from a clinical standpoint, too, the cardiac difficulties begin when the pregnancy begins and reach a point of maximum intensity four to six weeks before term. Therapeutic measures, therefore, to avoid decompensation must be instituted in the beginning of pregnancy. The "medically removable" burdens must be rigidly controlled from the very start; increased bed rest should be ordered from the first month of gestation, and absolute bed rest enforced when any suspicion of decreased cardiac reserve appears.

Clinical confirmation of the lightening of the cardiac burden in the last four to six weeks of gestation, suggested by the physiologic changes, has been sought for in our hospitalized cases. We have been so impressed with the improvement shown by rheumatic cardiac patients during the last month of gestation that we now anticipate it. Rarely is anything more than absolute bed rest ordered, withholding digitalis wherever possible, so that a clear-cut picture of the physiologic lightening of the circulatory burden the last month may be clinically observed. To date, we have had no reason to regret this relative inactivity, while, as a matter of fact, we feel that several cases have resulted in successful terminations only because of the waiting period, thus allowing the

physiologic improvement to exert its full beneficial effect. Of the several examples available only two of the more serious grades of cardiac decompensation will be reviewed.

CASE 1.—L. D. (History 17836), aged 42 years, para v, gravida vi, had rheumatic heart disease with enlarged heart, mitral stenosis, and insufficiency, Class 2B. She was digitalized and followed as an outpatient for approximately one month. She was admitted to the hospital because of a progressively decreasing capacity in the seventh month, complaining of cough, palpitation, dyspnea, orthopnea, and edema. Examination revealed many coarse rales throughout both lung bases, and marked edema. She could not tolerate any position in bed other than a 70 to 80 degree elevation of the back rest. The exertion of speaking caused obviously increasing distress. Moving from the bed to a stretcher in the eighth month resulted in extreme dyspnea and cyanosis. However, with no important change in medical care aside from most rigidly controlled rest, this patient managed to survive. Improvement occurred to an observable degree during the last few days of February, 1939. On March 7, 1939, the average ventricular rate was 72; ankle and sacral edema had disappeared. On March 18, spontaneous labor began. After fifty-two hours of difficult labor, this patient was delivered by midforceps. Her course during labor was splendid from a cardiac standpoint, as her pulse never rose above 90. The patient was discharged in relatively good condition on Apr. 12, 1939.

CASE 2.—R. E. (History 277), aged 43 years, para x, gravida x, had rheumatic heart disease with enlarged heart, mitral stenosis, and insufficiency with auricular fibrillation. The past history revealed at least three known attacks of cardiac failure during the past year. In fact, the patient became pregnant only a short time following discharge from another hospital where she underwent treatment for the third decompensation. On admission, in the tenth week of her pregnancy, her condition was quite similar to the case above described, with dyspnea, orthopnea, generalized edema, cyanosis, and fibrillation. Patient was digitalized and well rested. Months afterwards, digitalization and bed rest having been maintained, a Thanksgiving Day program with dinner, visitors, etc., was apparently sufficient to cause a severe attack of pulmonary edema. After seven months of absolute bed rest and only during the last few weeks of her pregnancy did this patient begin to achieve some degree of compensation. Spontaneous labor began on Feb. 26, 1938, and a cesarean section was performed shortly afterwards. Her postoperative course was remarkably smooth from a cardiac standpoint. When she was discharged on Apr. 4, 1939, in fair condition, she was able to carry out only the lightest of exertions. Three months later a fatal attack of decompensation occurred.

Both patients reviewed had cardiac failure in the early months of pregnancy. Both were desperately ill until the last month of gestation. Both improved in the last four weeks to a clinically demonstrable degree without any change in the therapeutic regime, one sufficiently to withstand a long labor and the other a cesarean section. As an obvious corollary, it has appeared logical to us to take advantage of the lightening of the load in the last month, to allow the gestation to go to term and to avoid late pregnancy interference when the circulatory burden is at its height.

The labor experience brought to light by the analysis of this series has materially influenced the management of patients with cardiac disease. Decompensation occurred during labor in only five instances. A careful review of these five cases has forced us to correct the incidence of failure in labor to one case in 345 deliveries. The following brief case abstracts give our reasons for this correction.

CASE 3.—H. H. (History 25666), aged 26 years, para 0, gravida i, had rheumatic heart disease with enlarged heart, regular sinus rhythm, mitral insufficiency and stenosis, Class 1. Patient attended our ante-partum clinic, and by error was considered to have a normal heart. She was admitted to the hospital in labor at term. After five and one-half hours of labor she suddenly developed acute pulmonary edema and hemoptysis. The cardiac disease was then discovered. A blood count, however, done just before delivery showed 2.5 million red cells and 50 per cent hemoglobin, the smear revealing many microcytes.

Improper clinic diagnosis and a marked secondary anemia of the microcytic type must also be considered in attempting to appraise this failure.

CASE 4.—V. L. (History 30780), aged 28 years, para 0, gravida i, had rheumatic heart disease with enlarged heart, mitral insufficiency and stenosis, regular sinus rhythm, Class 1. Patient was seen in the ante-partum clinic for almost seven months. Her complaint of cough during all this time was not considered seriously. She was admitted in labor at term. After thirty-nine hours of labor and immediately following an infusion of 500 c.c. of 25 per cent glucose, she developed pulmonary edema and severe cough, the ventricular rate jumping to 120. Rapid digitalization and a bloodless phlebotomy brought improvement, allowing a vaginal operative delivery later without complication.

It is our feeling that this individual was showing some evidence of decompensation for seven months prior to delivery, explaining the chronic cough, and that the relatively large amount of hypertonic solution given intravenously was sufficient to cause an acute episode.

CASE 5.—H. S. (History 37168), aged 30, para 0, gravida i, rheumatic heart disease with enlarged heart, mitral insufficiency and stenosis, regular sinus rhythm, Class 1. This patient suddenly developed acute cardiac failure after twelve hours of an otherwise normal labor.

This undeniably was an acute failure in labor.

CASE 6.—E. G. (History 31302), aged 20 years, para 0, gravida i, had rheumatic heart disease with enlarged heart, mitral insufficiency and stenosis, regular sinus rhythm, Class 2B. Patient was under clinic care and was admitted three weeks before term for bed rest. After four hours of normal labor an occasional rale was noted at the lung bases and what was called a slow fibrillation was reported. Immediately following delivery the ventricular rhythm was normal and no rales were heard.

This patient was not seen by a cardiologist and the evidence for cardiac decompensation is meager.

CASE 7.—A. H. (History 9889), aged 35 years, para iii, gravida iv, had rheumatic heart disease with enlarged heart, mitral stenosis and insufficiency, regular sinus rhythm, Class 2B. Patient was seen in the clinic in early pregnancy. In the sixth month of her pregnancy she complained of dyspnea and orthopnea, requiring three pillows for sleep, and had frequent nose bleeds. Patient returned in the seventh month, complaining of severe abdominal pain and bleeding. During a labor induced by bagging on account of uterine bleeding (placenta previa), a rapid pulse and basilar rales were noted.

On the chart this patient is diagnosed as an acute cardiac failure in labor. We feel that it cannot be denied that this individual exhibited definite symptoms of markedly decreased cardiac reserve in the sixth month of her pregnancy, severe enough to be classed as decompensation; and second, it should be noted that induction of labor was compelled

by an obstetric complication in the seventh month, when her circulatory burden was about at its greatest load.

Thus, it is our opinion that only one of these five so-called failures in labor may actually belong in this classification; one failure in labor in 345 cases, an incidence that impresses us as being no higher than the accident rate in rheumatic heart disease. The individual who has had the benefit of careful prenatal observation with preventive measures taken as indicated should enter labor compensated, and the onset of decompensation during labor need not be feared.

This brings us to the final consideration in this report, the value of cesarean section in heart disease. We know of no satisfactory quantitative estimation of the amount of work done during labor and the possible resultant strain on the heart. We know of no good way to estimate the burden placed on a heart by cesarean section and the postoperative period. An attempt was made to judge the effects of a normal spontaneous labor as compared to the effects of a cesarean section. The inadequacies of the following figures in answering this problem are fully realized by the authors. We have compared the convalescent periods of twenty-four cesarean sections to that of 304 vaginal deliveries, an unequal comparison at best, but reflecting our tendency in management.

TABLE V. CONVALESCENCE: CESAREAN SECTION VS. VAGINAL DELIVERY

	CESAREAN SECTION	VAGINAL DELIVERY
Total	24	304
Fever more than 3 days	7 — 29.1%	13 — 4.2%
Pulse over 90 more than 3 days	21 — 87.5%	105 — 34.5%
Fever more than 5 days	5 — 20.8%	8 — 2.6%
Pulse over 90 more than 5 days	18 — 75.0%	59 — 19.4%

The post-partum period in women who have had a cesarean section is accompanied by elevated temperature and pulse readings much more often than in patients who have had a vaginal delivery. The possibility of vomiting, abdominal distention, and pain with their concomitant strain upon the heart must also be carefully appraised in judging the burden to the patient of a cesarean section compared to a vaginal delivery.

The mortality rates are compared in Table VI.

TABLE VI. MORTALITY: ABDOMINAL OPERATIVE DELIVERY VS. VAGINAL DELIVERY

	CESAREAN SECTION AND HYSTEROTOMIES	VAGINAL DELIVERY INCLUDING SPONTANEOUS ABORTIONS
Total	29	314
Deaths	4 — 13.8%	6 — 1.9%
Corrected	2 — 6.9%	4 — 1.2%

Four deaths occurred in the operative group, an incidence of 13.8 per cent. Two of these deaths may be discounted, one being sectioned at the moment of death in an attempt to save the fetus, the other only after the patient's condition was considered hopeless. Of 314 vaginal deliveries, including four spontaneous abortions, 6 died, a mortality of 1.9 per cent. This may also be corrected. One patient was delivered spontaneously, her cardiac condition undiagnosed at this

time. Two months later she was readmitted because of femoral thrombophlebitis. The complicating cardiac condition was now diagnosed for the first time, and she died later as a result of pulmonary embolism. A second patient, B. B., died in cardiac failure when eighteen weeks pregnant. The fetus was expelled just at the moment of death.

We do not intend to draw any conclusions from these figures in favor of or against any particular form of delivery. Each case presents an individual problem. However, we feel that it is of some interest to report that our most serious cardiac patients, i.e., the 5 patients grouped as Class 3, were delivered by the vaginal route. May it be stressed that they were considered too serious cardiac risks to be offered the "benefits" of cesarean section. One patient mentioned above, B. B., died in her fourth month; the other 4 survived. With the incidence of morbidity and the mortality rate significantly higher following cesarean section, and since cardiac failure is a rarity during labor, it has been our policy to favor, from a cardiac standpoint, vaginal delivery.

SUMMARY AND CONCLUSIONS

1. Three hundred forty-five cases of pregnancy complicated by rheumatic heart disease are reported.

2. Seventy-seven cardiac failures occurred in this group, an incidence of 22.3 per cent. We feel that it is possible to foretell fairly accurately which patient with heart disease will fail unless adequate bed rest is enforced. Several prognostic aids are offered.

a. The functional capacity of the heart in the nonpregnant state is of great importance, 83 per cent of the failures occurring in the badly incapacitated groups, 2B and 3, while only 17 per cent of the failures were in the comparatively well-functioning Classes 1 and 2A.

b. An equally important aid is the patient's age; 42.6 per cent of the pregnancies in women over thirty years of age were complicated by cardiac failure as compared to 16.1 per cent in the group under thirty.

c. A third significant aid in prognosis is the presence or absence of a history of previous failure. Of those that decompensated before, 75 per cent had cardiac failure when pregnant as compared to a 14.1 per cent incidence of cardiac failure in the previously compensated group.

We feel, therefore, that the patient whose measure of functional capacity places her in the relatively severe grades of heart disease, the cardiac patient who is more than thirty years of age, the cardiac patient who gives a history of previous decompensation, should be willing, if she wishes to assume the burden of pregnancy, to submit to frequent antenatal observations from the very beginning of her pregnancy and she must be willing and able to spend the greater part of the pregnancy at absolute bed rest if necessary. The number of pregnancies borne by women with rheumatic heart disease, in itself, is apparently of no consequence. The multigravid, however, will more commonly fall into one or more of the three groups mentioned above.

3. The incidence of cardiac failure in pregnancy can be reduced markedly if the general principle of early and absolute bed rest is adhered to. We have had two failures in our last 103 cases, and one of these was possibly preventable.

4. Eighty per cent of the 77 cardiac failures that were seen at this hospital occurred before the last month of gestation. Acute failure during labor is a rarity. Our clinical experience follows very closely the physiologic changes which indicate that pregnancy exerts a steadily increasing circulatory burden, beginning when the pregnancy begins and reaching a maximum during the eighth month. A lightening of this circulatory load occurs during the period four to six weeks preceding delivery with a consequent clinical improvement. Therefore, we feel it unwise to resort to late pregnancy terminations and follow the general rule of allowing the gestation to go to term.

5. Each pregnancy presents an individual problem in the management of labor. In our series, 8.4 per cent of the patients were delivered by the abdominal route and 91.5 per cent were delivered vaginally. Since the incidence of morbidity, as expressed by fever with its concomitant elevation in pulse rate, and the mortality rate are significantly higher following cesarean section; and since cardiac decompensation is a rare accident during labor, we feel that the "burden of proof" lies with cesarean section. This consideration applies only to section for the cardiac condition "per se." Patients who have had the benefit of treatment, and go into labor well compensated, may in general be handled on the basis of obstetric indication, essentially as though not suffering from heart disease.

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These three patients had typhoid fever associated with vaginal or uterine bleeding. Incidentally, because of this bleeding two of these patients had been assigned to the gynecologic ward. In all three cases *B. typhosus* had been obtained in pure culture and the Widal had been positive although only later in the disease. All three patients had an irregularity of the menstrual cycle; one had metrorrhagia during the first and second weeks of the disease; one had menorrhagia and the third patient had an abortion five months previously, but the typhoid fever was ushered in by profuse bleeding. This latter patient died and autopsy revealed a typical nonpregnant uterus with no evidence of remnants of a pregnancy.

The authors believe that the excessive uterine bleeding in these patients was a part of the disease, and did not represent the rare hemorrhagic type of typhoid fever. The importance of the symptom of vaginal bleeding lies in the possibility of confusion in diagnosis. Therefore, menorrhagia and metrorrhagia should be borne in mind in the diagnosis of typhoid fever in women. Abnormal uterine bleeding in typhoid fever probably is encountered more frequently than the literature would indicate.

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THE EFFECT OF PREGNANCY ON EXPERIMENTAL HYPERTENSION*†

With Observations on the Effects of Deciduomas

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WOMEN who begin pregnancy with arterial hypertension usually undergo a progressive rise of blood pressure as the pregnancy advances. This is true with essential hypertension, and is particularly true in cases of chronic Bright's disease. Severe hypertension of any origin is considered by Herrick[1] and many others to be a strong indication for therapeutic abortion. Exceptional cases occur of hypertensive women whose blood pressure declines during pregnancy.

In order to study the factors which might be responsible for this unfavorable influence of pregnancy upon human hypertension, it would seem important to examine the effects of pregnancy upon both the course and the onset of hypertension induced experimentally in animals.

Few observations on this subject have been reported. Dill and his collaborators[2] have stated that dogs and rabbits are more susceptible to renal ischemia during pregnancy, both species developing an "eclamptic-like syndrome characterized by hypertension, albuminuria, coma, convulsions and death," and that such a syndrome did not occur in their nonpregnant control animals. Goldblatt, Kahn and Hanzal,[3] on the other hand, found that pregnancy produced a slight or moderate fall of blood pressure in hypertensive dogs, and they attribute this to the compensatory action of the fetal kidneys. Similar observations on dogs have been made by Dawson, Cressman and Blalock[4a] and by I. H. Page.[4b] In hypertensive rats a lowering of blood pressure during pregnancy was recorded by Harrison, Grollman and Williams,[5] and they likewise attributed the effect to an antipressor action of the fetal kidneys. Indeed, Goldblatt[6] states that pregnant dogs can withstand a degree of renal ischemia which nonpregnant females would be unable to tolerate.

There is, then, a lack of agreement as to the effect of pregnancy upon the course of experimental renal hypertension, and there is much uncertainty as to the interpretation of the various findings.

METHODS

Rats and rabbits were used because of their convenient breeding habits. The rabbits were kept in individual cages on a diet containing 12 per cent protein. Blood pressure was determined on the central artery of the ear by the method of Grant and Rothschild[7] without anesthesia. Pregnancies were induced at the proper time by mating with bucks of known fertility, and pseudopregnancies were induced by

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mating with sterile bucks. In rabbits hypertension was produced by partial ligation of the renal arteries, following the details described in a previous communication.[9]

The rats, of the Long-Evans strain, were housed in groups of four and maintained on a diet containing requisite food factors including 18.5 per cent protein. Blood pressure was measured without anesthesia by the tail plethysmograph method described by Williams, Harrison and Grollman.[8] In rats persistent hypertension was produced in two ways: (a) By partial ligation of one renal artery to 0.3 mm. according to the technique of Wilson and Byrom,[10] using a silk ligature over a wire of known diameter; and (b) by our own modification of a method similar to that used on dogs by I. H. Page[11] and by Greenwood, Nassim and Taylor.[12] The technique consists of painting one kidney (explanted subcutaneously to avoid intestinal adhesions) with collodion and removing the opposite kidney one to four weeks later. Each method produced sustained hypertension in about two-thirds of all operated rats.

In some instances pregnancy was induced after the blood pressure had reached a hypertensive level; in other instances the renal surgery was performed at various stages of pregnancy in order to compare the results with those of Dill and Erickson.[2] It was noted that many hypertensive rats were refractory to mating because of a cessation of estrus cycles, the latter finding having been noted by Diaz and Levy.[13] Since all of the hypertensive rats lost some weight, and since this estrus inhibition was particularly noticeable in those which lost a great deal, its mechanism is probably the same as that described for inanition,[14] namely, a failure of the hypophyseal gonadotropic function. In some animals, therefore, 10 rat units of gonadin were injected to induce estrus. In a further group of 12 hypertensive rats, pseudopregnancies were induced by stimulation of the cervix with a glass rod or an electric current. Deciduomas were then produced by placing four or five silk threads through each uterine horn four to five days after induction of pseudopregnancy. The existence of the placentomas was checked later by exploratory laparotomy.

RESULTS

1. *Blood Pressures of Normal Rabbits and Rats, and the Criteria for Hypertension.*—The normal systolic pressure in the ears of the rabbits used varied from 70 to 103 mm. Hg (median value 76). Since the values are fairly constant for any one rabbit, a rise greater than 20 mm. Hg above the basal level maintained for two consecutive occasions on different days was accepted as hypertension.

The mean of the tail blood pressures on a random sample of 21 rats, using the last 3 of 7 biweekly readings on each rat was 104 mm. Hg with a standard deviation of 5. Rats giving three consecutive readings over 120 (three times the standard deviation above the mean) several days apart were considered hypertensive. The hypertension following unilateral renal artery constriction was sometimes marked (over 200 mm. Hg) and persisted indefinitely (six months or more). The rats thus differ from dogs and rabbits in which the presence of a normal kidney usually causes a disappearance of the hypertension. In three rats with marked hypertension and rapid wasting, the blood ureas were found to be only slightly elevated (62 mg. per cent); so marked azotemia is not necessarily present in this type of hypertension.

2. *Normal Animals During Pregnancy.*—There have been numerous studies of the effect of pregnancy on the blood pressure of normal women (summarized by Jensen[15]), and although there is no significant change in the systolic pressure, there is a slight lowering of the diastolic pressure. We have found no references regarding the effect of pregnancy on the blood pressure of any animals except for our own studies[16] on rabbits in which we found the blood pressure unchanged. The influence of pregnancy on the blood pressure of normal rats is being investigated further.

3. *Renal Ischemia Induced During Pregnancy.*—In a group of 18 rats, the left renal artery was constricted to 0.3 mm. under identical conditions. Eight of these animals were in various stages of pregnancy at the time of surgery, six becoming hypertensive. The important finding was a delay in the onset of hypertension until

after parturition, compared with the usual rapid onset (see Figs. 1 and 2). This suggests that rats are less susceptible to renal ischemia when pregnant. In rabbits, our experience indicates that the effects of partial ligation of the renal arteries are no different in pregnant than in nonpregnant animals.

4. *Pregnancy in Hypertensive Rabbits.*—In 12 rabbits, pregnancy was induced after the production of hypertension by the methods outlined. Nine showed no consistent change during pregnancy and in three there was a slight fall.* Four

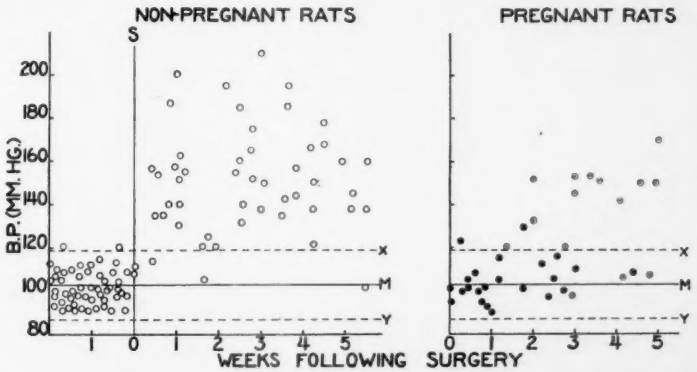

Fig. 1.—Delay in onset of hypertension following renal ischemia produced during pregnancy. ○, nonpregnant rats. ●, pregnant rats. ⊙, post-partum rats. This notation continues through all the figures. Ordinate *O* represents surgery. The value *M* is the mean normal blood pressure for a group of 21 rats. Lines *x* and *y* are ± 3 standard deviations from this mean (see text). Note that nearly all the measurements in the first week following surgery are hypertensive in the nonpregnant group, whereas only 1 reading in the first week is hypertensive in the group of pregnant rats.

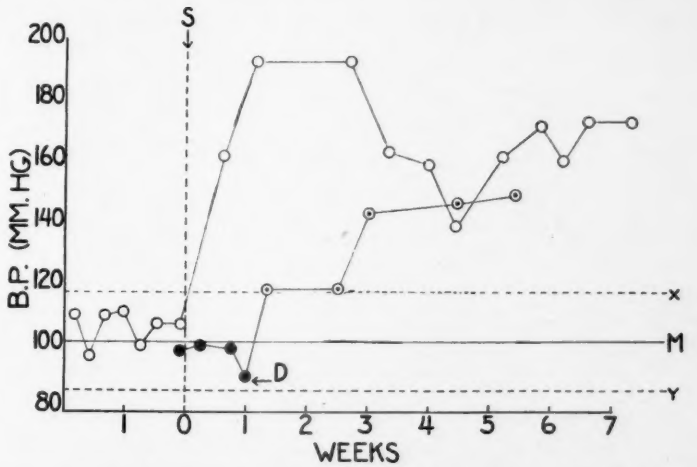

Fig. 2.—Comparison of immediate effect of renal ischemia on a pregnant and a nonpregnant rat. Symbols as in Fig. 1. *D*, represents day of delivery.

of these experiments are illustrated in Fig. 3. Neither the blood pressure changes, the appearance of the animals, nor their behavior differed in these hypertensive pregnant rabbits from those observed in the normal pregnant rabbits previously reported.[16]

5. *Comparison of Effects of Pregnancy and Dietary Load in Rabbits With Limited Renal Blood Supply.*—The above 12 rabbits were subsequently placed on a

*In an independent study, as yet unpublished, Dr. John D. Corbit at the University of Pennsylvania Medical School has essentially the same findings.

diet enriched with enough casein to double the original (12 per cent) protein content. Whereas pregnancy had not affected them adversely, the increase of dietary protein caused illness and death in a third of the animals. This indicates that increasing the load on the ischemic kidney produces detrimental effects which these same animals had not shown during their pregnancies.

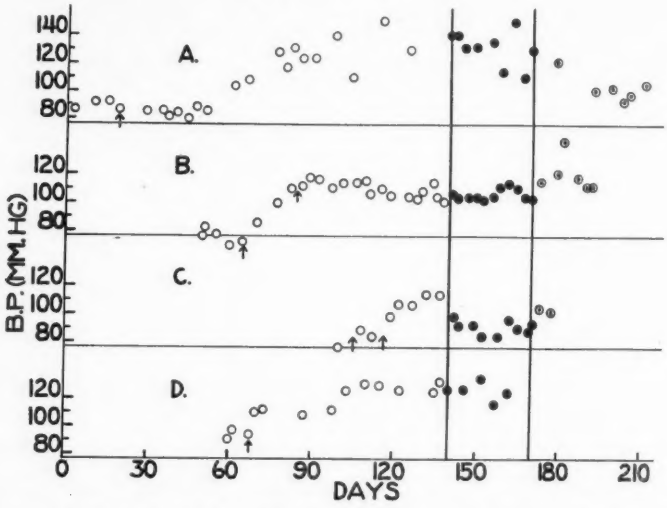

Fig. 3.—The influence of pregnancy on rabbits with experimental hypertension. Serial observations on 4 selected animals. Notations as in previous figures. Arrows indicate surgery. Vertical lines indicate beginning and end of pregnancy.

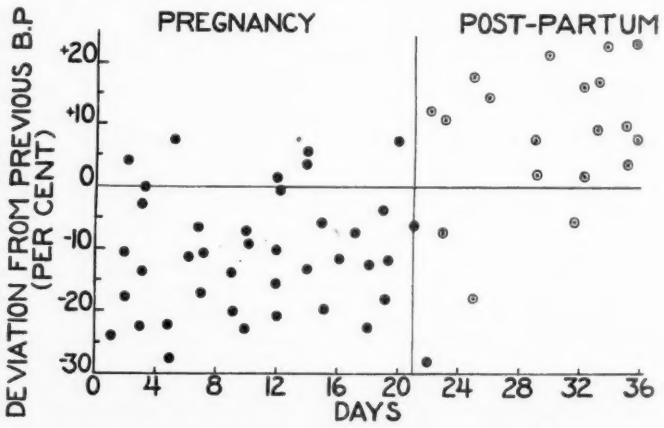

Fig. 4.—Influence of pregnancy on previously hypertensive rats. Notations as in previous figures. All values are expressed as a percentage deviation from the mean of the 3 readings immediately preceding mating for each animal. Note the return to a hypertensive level following delivery (vertical line at twenty-one days). Ordinate *0* represents day of mating.

6. *Pregnancy in Hypertensive Rats.*—Ten of the hypertensive rats were successfully mated and their blood pressures followed during pregnancy and the puerperium. In every case there was a definite fall of blood pressure during pregnancy with a return after delivery. This fall was often observed during the first third of pregnancy, even before implantation of the ovum occurs. In Fig. 4, illustrating this phenomenon in the whole group, it may be seen that almost all of the observations during pregnancy fall below the zero line, which represents the mean of three readings taken immediately before pregnancy in each rat.

7. *Pseudopregnancy With Deciduomas in Hypertensive Rats.*—The behavior of the blood pressure in a group of 11 rats, in which deciduomas were produced, showed a very striking resemblance to that of the pregnant animals, as may be seen by a comparison, of Figs. 4 and 5. Note that the decline in blood pressure occurred within a few days after induction of pseudopregnancy, often before the threads were placed through the uterus. When stimulation of the cervix did not induce pseudopregnancy, and the insertion of threads in the uterus did not produce deciduomas, as shown by subsequent laparotomy, such a decline of hypertension did not occur.

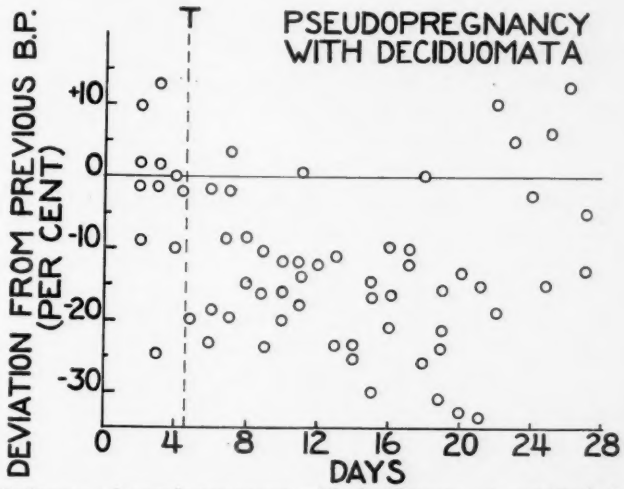

Fig. 5.—Influence of pseudopregnancy with deciduomas on previously hypertensive rats. Details of legend as in Fig. 4. Ordinate *O* represents artificial induction of pseudopregnancy. Note tendency to return toward the hypertensive level during the fourth week. On the fifth day following artificial induction of pseudopregnancy (ordinate *T*) threads were placed in the uterine mucosa to produce deciduomas.

DISCUSSION

It would seem that rats and rabbits are less susceptible to renal ischemia when pregnant inasmuch as it has been found more difficult to produce hypertension during pregnancy. The findings are in contrast to those reported by Dill and Erickson[2] but support the observations of Goldblatt.[6] Pregnancy, furthermore, lowers the blood pressure in experimental renal hypertension, although the effects are more pronounced in rats than in rabbits. This is remarkably at variance with the often disastrous influence of pregnancy upon renal hypertension in women. If this is truly a species difference, it is very important to know what factors account for it.

There are several possible explanations for the lowering of blood pressure during pregnancy in hypertensive animals. First, there is the explanation advanced by Goldblatt[3] and by Harrison, Grollman and Williams[5] that the fetal kidneys cause a lowering of the hypertension through some compensatory action. This explanation, however, could not account for the decrease in the hypertension which we found to follow the onset of pseudopregnancy with deciduomas in rats; nor could it explain the decrease in hypertension which was found to precede the implantation of the ovum and to precede by far the development of a

functioning kidney. It is therefore necessary to search for another explanation.

Another point of view which has not hitherto been adequately considered concerns the relationship of the degree of hypertension to variations in the load on the kidneys during pregnancy. The feeding of high nitrogen diets to hypertensive animals has been said to cause a rise of blood pressure[17] or an increased mortality (see pages 55 and 56) presumably because of the increased nitrogenous load on the kidneys. During pregnancy, however, due to the marked storage of protein with resulting diminution of nitrogen output, the load on the kidneys may actually be decreased. It has been shown by Walter and Addis,[18] for example, that the ratio of kidney weight to body weight, which is one index of renal work, is considerably less in pregnant rats at term than in normal controls. Nitrogen balance studies on normal pregnant women have shown an actual decrease in the nitrogen output and there is, in addition, a lowered nonprotein nitrogen level in the blood. Inasmuch as the real osmotic work of the kidney is nearly proportional to the nitrogen excretion,[19] it would seem that pregnancy alone would not constitute a "burden" upon the excretory function of the kidneys even in human beings.

This point may be unsettled, but the statements by Kellogg,[20] Dieckmann,[21] Stander,[22] and indeed in most textbooks on obstetrics, that the exacerbation of hypertension in nephritis is due to the "burden of pregnancy on the kidneys" might well undergo critical re-examination. The direction of change in osmotic work imposed upon the kidneys during pregnancy may, of course, vary with the amount of protein in the diet, but the magnitude of such alterations would be small and probably negligible. The contrast between human beings and the experimental animals here considered makes it unlikely that this is the principal factor involved. Certainly one must look for some other factor to explain the almost invariable increase of hypertension in pregnant women in view of the almost invariable reduction of hypertension in pregnant or deciduomatous rats.

The concept that a "low reserve kidney" might account for a rise of blood pressure during late pregnancy is still firmly entrenched in obstetric literature. Certainly the partial renal artery ties, subtotal nephrectomies and other procedures utilized for the production of hypertension constitute experimentally produced kidneys of "low reserve." Even though the hypertension of rabbits may have subsided, we have shown above that loading their kidneys with an increase in dietary protein may cause sickness and death; yet pregnancy alone even in the same animals will cause neither.

A third explanation for the lowering of experimental hypertension during pregnancy concerns the hemodynamic changes which follow the insertion of placentas into the circulatory apparatus. The placentas of rats, rabbits, and human beings, though differing somewhat in vascular arrangement,[23] may all constitute a low resistance shunt which decreases the peripheral resistance and probably accounts for the lowering of diastolic pressure during normal pregnancy. Such a concept has been

emphasized by Burwell.[24] This circulatory factor is by no means eliminated, since it is also probably active when the highly vascular deciduomas are induced in rats.

Common factors which do exist in all three conditions (i.e., pregnancy, pseudopregnancy, and deciduomas) are the endocrine changes which are at least qualitatively similar. It would seem likely therefore that such endocrine changes might be concerned with the lowering of blood pressure. Inasmuch as the human placenta secretes its own gonadotropic hormone[25] which is not known to be produced by the placentas of animals other than primates, this is one difference between pregnancy in rodents and women which should receive due consideration. Experiments are in progress to determine the effects of pseudopregnancy alone and of the various sex hormones upon the blood pressure of hypertensive animals. There is very likely some humoral relationship between the placenta and the kidney, a relationship which may be of some importance in the study of the hypertensive disorders of pregnancy.

CONCLUSIONS

1. Pregnancy appears to have a beneficial effect upon experimental renal hypertension in the rat or rabbit.

2. When operations designed to limit the blood flow to the kidney are performed *during* pregnancy, the onset of hypertension is commonly delayed until after parturition; whereas it usually appears within a very few days after surgery in nonpregnant controls.

3. Pregnancy does not constitute a "burden" on the kidneys. This is indicated by the fact that animals with minimal amounts of functioning kidney tissue (i.e., experimentally produced "low reserve kidneys") do not exhibit hypertension during pregnancy, but when not pregnant may die when the excretory work of the kidneys is increased by adding more protein to the diet. Some factor other than increased renal work or "load" must explain the difference between hypertensive animals and hypertensive women during pregnancy.

4. Pseudopregnancy with deciduomas likewise lowers the blood pressure of hypertensive rats.

5. The possibility is suggested that either the endocrine or the circulatory changes associated with pregnancy, pseudopregnancy, or the decidual tumors are responsible for this effect, rather than any compensatory action of fetal kidneys.

SUMMARY

To shed light on factors possibly concerned with the unfavorable influence of pregnancy upon human hypertension, rats and rabbits with experimental hypertension were studied during pregnancy or pseudopregnancy with deciduomas.

Blood pressures were measured in rats by the tail plethysmograph and in rabbits by the ear capsule method. Hypertension was induced by partial ligation of renal arteries, or in some rats by painting one kidney with collodion and removing the opposite kidney later. Deciduomas were induced by placing silk threads in the uterine mucosa during pseudopregnancy.

During pregnancy in normal rabbits, the changes in blood pressure as shown by these methods are negligible. Renal ischemia produced during pregnancy was followed by hypertension, but the onset was delayed until after delivery. Pregnancy produced an early fall in blood pressure in all of 10 hypertensive rats and a less constant fall in 12 hypertensive rabbits. No untoward effects were observed. An increase of protein content in the diet caused sickness or death in hypertensive nonpregnant rabbits. Pseudopregnancy with deciduomas in all of 11 hypertensive rats caused a decline in blood pressure corresponding roughly in time and extent with that caused by pregnancy.

These findings suggest that the cause for the blood pressure fall observed more likely results from endocrine changes than from any action of fetal kidneys. Doubt is thrown on the concept that a "load on the maternal kidneys" plays a significant part in the exacerbation of hypertension usually observed in human pregnancy.

The authors are indebted to Drs. Tinsley, Harrison, F. W. Hartman, L. V. Dill, and H. Selye, for their valuable comments and suggestions.

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II. THE CLINICAL AND LABORATORY DIFFERENTIATION OF SPONTANEOUS AND INDUCED ABORTION*

A Study of 502 Cases

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THE diagnosis of abortion is beset with several minor and one major difficulty. Ordinarily, the familiar history of a period of amenorrhea followed by abdominal cramps, vaginal bleeding, and the passage of clots with or without a recognizable fetus makes it clear that conception has occurred and that the normal course of gestation has been interrupted at an early stage. Ordinarily, it is also easy to determine whether the abortion is threatened, inevitable, incomplete, complete, or missed.

In a fair number of cases, however, one may be misled in arriving at even this simple diagnosis. Ectopic pregnancy may masquerade for a time as threatened or inevitable abortion. Hydatidiform mole may do the same. Menorrhagic and metrorrhagic conditions unassociated with pregnancy may lead to errors in diagnosis as may also the first hemorrhagic episode of a submucous fibroid or carcinoma of the corpus.

But to differentiate between spontaneous and induced abortion is the major difficulty. This is one of the rare instances in which the patient usually knows the diagnosis and the physician does not. If patients always told the truth there would be no problem. Everyone who has had experience with the aftercare of abortion is aware, however, that a patient who is perfectly frank and trustworthy about all other matters may lie blandly and persistently on this point alone. And it is a point of great significance for the management of the case and for its prognosis. Many authorities go so far as to say that the patient's statement per se is worthless unless she admits induction. The inference that induced abortion is far more frequent than hospital records indicate is almost universal.

A remarkable exception is found in Pearce,[1] who states that in the neighborhood of St. Giles Hospital, London, where his study was made, emmenagogue pills are taken as routinely for delayed menstruation as laxatives for constipation. He goes on to state his belief that "induced abortion is certainly much less frequent than these figures taken at their face value would suggest. Idiopathic abortion is so common and the human characteristic of rationalization so strong that any estimation of the proportion of criminal abortion is well nigh impossible. Many of the noxious things were taken and done in innocence, sometimes the woman not knowing she was pregnant." This is the view that would consider any abortion spontaneous until proved to be induced. It is rare. The reverse is

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usually held. Most recent writers have wisely abandoned the old, simple and patently fallacious method of considering fever proof-positive of illegal interference. Bouleware,[2] Pasmore,[3] Simons,[4] and others have pointed out the presence of septic signs in incomplete spontaneous abortion with sapremia. Cook[5] observed a typical septic course in a patient who aborted spontaneously while on the medical ward under treatment for cardiac disease. Studdiford[6] in an earlier study reported two similar cases.

By whatever path one approaches the task of classification on this point it becomes evident that no clear-cut grouping can be made. The group who frankly admit mechanical induction may be taken as the "purest" from which one should be able to derive criteria for determining objectively the truth or falsehood of a claim to spontaneous abortion. Unfortunately no such clear-cut criteria can be so derived. While statistically this group does show a higher frequency of fever, low sedimentation rate, acute inflammatory reaction in decidua and chorion, etc. (Tables I and II), there are individual cases which exhibit none of these. On the other hand, all of these evidences of infection are to be found among those who most convincingly deny any kind of intentional interference. A clean curettage by a skilled abortionist is obviously no more liable to infection than a therapeutic abortion performed in our own operating room. Conversely, an incomplete spon-

TABLE I. PATIENT'S STATEMENT OF TYPE OF ABORTION, EXAMINER'S ESTIMATE OF VERACITY, PATIENTS WITH TEMPERATURE 100.4° F. OR ABOVE, PATIENTS WITH SEDIMENTATION RATE LESS THAN 40, PATIENTS TREATED BY CURETTAGE

TYPE OF ABORTION	CASES	%	FEBRILE	%	LOW SR	%*	CURETTED	%
Induced (mechanical)	52	100	18	35	19	44	30	59
Spontaneous (false)	32	100	8	33	14	50	18	59
Spontaneous (doubtful)	156	100	32	22	43	35	101	64
Induced (drug)	104	100	20	18	32	35	71	68
Spontaneous (true)	158	100	24	14	25	20	113	71
Totals	502	100	102	20	133	26	333	67

*Per cent of cases in which sedimentation rate was reported.

TABLE II. STATED INDUCTION BY PATHOLOGY REPORT

PATHOLOGIC DIAGNOSIS			DIAGNOSIS FROM HISTORY					
	CASES	%	INDUCED (MECH.)	%	INDUCED (DRUG)	%	ALL SPONTANEOUS	%
No report (not curetted)	170	34	21	41	34	32	115	33
Acute inflammation of decidua and chorion	53	10	10	18	9	9	34	10
Degeneration of decidua and chorion	204	41	15	29	48	46	141	41
Normal pregnancy	9	2	1	2	3	3	5	1
Normal endometrium	25	5	1	2	3	3	21	6
Endometritis	15	3	1	2	2	2	12	4
Cystic and glandular hyperplasia	4	1	--	--	1	1	3	1
Placental polyp	13	2	--	--	3	3	10	3
Endometrial polyp, endocervicitis, etc.	6	1	1	2	1	1	4	1
Autopsy, only*	3	1	2	4	--	--	1†	--
Totals	502	100	52	100	104	100	346	100

*In 2 cases death was preceded by curettage. Total autopsies 5.
†Not pregnant.

taneous abortion offers the same nidus as retained secundines post partum. The uterus recognizes no moral distinctions.

Even microscopic study of curettings does not answer the question, "Induced or spontaneous?" although it sometimes corrects the clinical diagnosis of "abortion." Four cases, typical of many, serve to illustrate this point.

CASE 1.—(Fig. 1.) M. B., married, aged 22, para i, gravida ii, bled for three weeks at the fourth month of her previous pregnancy and was treated for threatened abortion by hospitalization at New York Women's Infirmary. She carried to term and was delivered of a normal child. Last menstrual period occurred on March 10, 1938. This was a planned pregnancy. She was cleaning house on May 28,

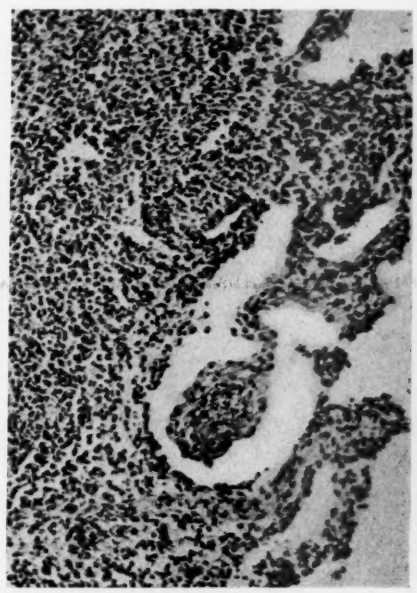

Fig. 1.

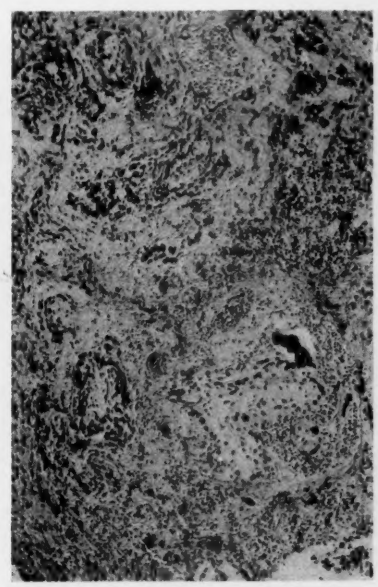

Fig. 2.

Fig. 1.—Degeneration and acute inflammation of the decidua.
Fig. 2.—Marked degeneration of decidua and early placenta.

and became dizzy and began to bleed at 7 P.M. At 9 P.M. severe cramps began and the next day clots were passed. Curettage on May 31 revealed degeneration and acute inflammation of the decidua. This patient gave a most convincing history of spontaneous abortion. Her course while in the hospital was afebrile; white blood count 10,100, polymorphonuclear leucocytes 62 per cent; sedimentation rate one hour; Wassermann negative; hemoglobin 80 per cent.

CASE 2.—(Fig. 2.) J. D., married, aged 30 years, para ii, gravida iii, had her last menstrual period on Dec. 28, 1938. She had used no contraceptive. She did a heavy washing, took a hot bath, and a dose of castor oil to induce abortion on March 6, 1939. This was followed immediately by the onset of cramps and spotting. On March 9 bleeding became profuse and clots were passed. Curettage on March 10 revealed marked degeneration of decidua and early placenta.

CASE 3.—(Fig. 3.) I. P., married, aged 23 years, para 0, gravida 0, had her last menstrual period on Oct. 3, 1938. Menstrual periods previously had been regular. She suffered a fall on December 3 and immediately had cramps and spotting fol-

lowed on the same day by profuse bleeding and the passage of clots. Curettage on December 4 revealed a normal early proliferative endometrium.

CASE 4.—(Fig. 4.) M. B., married, aged 33 years, para i gravida ii, had her last menstrual period on April 15, 1938. She had planned for this pregnancy. On June 20, for no apparent reason, she began spotting and having cramps. Three hours later bleeding became profuse and the next day several large clots were passed. Curettage on June 24 revealed cystic and glandular hyperplasia of the endometrium.

We can proceed then to a statistical analysis of admittedly impure groups, recognizing the probability that an indeterminate number included in the spontaneous group have actually undergone some form of mechanical interference, but with the growing conviction that the proportion of these is probably smaller than some authors have supposed.

Fig. 3.

Fig. 4.

Fig. 3.—Normal early proliferative endometrium.
Fig. 4.—Cystic and glandular hyperplasia of endometrium.

The cases upon which this study is based were 502 patients admitted to Bellevue Hospital because of illness associated with the early interruption of pregnancy. I[7] have already reported the sociologic and psychologic characteristics of this group. The 35 cases of therapeutic abortion included in the previous series have been excluded from the present one, which consists of 346 (69 per cent) who claimed to have had spontaneous abortions, 104 (20.7 per cent) who admitted having used medical means to interrupt an unwanted pregnancy, and 52 (10.3 per cent) who confessed to mechanical interference.

Those who admit induction by means of drugs present an interesting situation. In the first place the group probably includes a number whose induction was actually mechanical. This is because drug induction does not seem to carry with it the same moral odium as does me-

chanical interference, and also because its admission does not implicate the abortionist whom the woman, whether from fear or gratitude, feels compelled to shield. Second and far more important, this group, on statistical analysis, shows highly significant correlations with that which we have classified as "spontaneous-true," i.e., that in which any kind of induction was most convincingly denied. Two groups classified according to the investigator's impression of the patients' reliability as "spontaneous-false" and "spontaneous-doubtful" assume intermediate positions. Reference to Table I will make clear the gradations from "induced-mechanical" to "spontaneous-true" and will show that according to these criteria "induced-drug" belongs almost at the opposite pole from "induced-mechanical." Whatever the patients' motives and intentions, she has in all probability undergone a spontaneous abortion coincidental with, but only slightly, if at all, influenced by the efforts she has made to avert the birth of an unwelcome child. In the "induced-drug" group are included not only those who took various medications by mouth but also those who soaked in hot baths and plied themselves with douches and enemas. (Douches in which the patient thought the nozzle had entered the cervical os and reported an immediate uterine cramp were considered mechanical interference.)

This finding furnishes strong confirmation of the opinion that efforts which fall short of invasion of the uterus are powerless to expel normal products of conception from a woman who is not predisposed to abort. Patients in whom such invasion is neither admitted nor strongly suspected correspond statistically in all ways, except the purely psychologic, to the spontaneous group. This is a point of major importance for treatment and prognosis.

The patient's statement as to whether her abortion was spontaneous or induced is not the only point in the history which can give a clue to the actual condition. Obviously a history of debilitating disease or of trauma should be given some weight, though these are perhaps fully as likely to figure in the fiction of one who would conceal induction as in the straightforward story of one who has lost her fetus involuntarily.

Of the 346 patients who claimed that abortion was spontaneous, 105 (30 per cent) could assign no cause for the onset of symptoms; 123 (36 per cent) spoke of over-exertion: climbing stairs, heavy lifting, laundry work, and the like; 47 (14 per cent) could point to some trauma such as a fall or a blow on the abdomen; violent emotions, especially fear or anger, were mentioned by 19 (5 per cent); and 52 (15 per cent) named a variety of other precipitating factors: coitus, heat, cold, malnutrition, "weakness," etc. It is curious that these various "causes" were distributed with equal frequency throughout the months of early pregnancy. It seems likely that, at least statistically, they may have been rationalizations in the same sense as in the drug inductions. There can be little doubt that abortion may be precipitated by any one of them, but whether this can occur with a healthy fetus in a woman not predisposed to abort is another question.

The history of previous spontaneous abortions offers evidence in support of the contention that the current one is also spontaneous. One-

third of the patients who claimed to have had a spontaneous abortion at this time and who had previously been pregnant gave a history of one or more previous spontaneous abortions. Only 10 per cent of previously gravid patients who admitted mechanical interference in the current pregnancy presented such a history. Twenty-nine per cent of the latter, however, admitted previous mechanically induced abortion while but 5 per cent of the former did so. This fact is opposed to the belief sometimes voiced that induced abortion is likely to be followed by "miscarriage" in subsequent pregnancies.

It is often said that first pregnancies are more likely to terminate in spontaneous abortion than are subsequent gestations. This statement is not confirmed by the present data. In our series there were 114 primigravidas. Thirty-two per cent admitted induction and 68 per cent denied it. Of the 388 patients who had previously been pregnant, 74 (19 per cent) gave a history of abortion in their first pregnancy. Fifty-three (71 per cent) said that this termination was accidental, or in other words, 13 per cent of first pregnancies in the previously gravid group ended in spontaneous abortion. These 388 women had had an aggregate of 1,240 pregnancies prior to the current gestation. Of the 852 pregnancies which were of higher order than the first, 245 (27 per cent) ended in abortion. One hundred thirty-six (55 per cent) were said to be spontaneous, 109 (45 per cent) induced abortions. If the pregnancies voluntarily interrupted are excluded from the calculation, we find that 17 per cent of all pregnancies of higher order than the first ended in spontaneous abortion. It must be supposed, for reasons already stated, that a certain number of the past abortions reported as induced were in reality spontaneous. The reverse is not nearly so likely in the past history as in that relating to the current illness.

Turning from the history to the clinical course, we find that 35 per cent of the group admitting mechanical induction had temperatures of 100.4° F. or over, while the spontaneous and drug-induced groups each had but 18 per cent febrile cases. The former group had proportionally four times as many patients with temperatures above 103° F. as the two latter groups. Only 14 patients in the entire series, however, exhibited this grade of pyrexia.

Hemorrhage played a minor role in the morbidity of these patients. In spite of the ready availability of bank blood for transfusion, this procedure was thought advisable in only 14 cases. Only 19 patients exhibited hemoglobins of 50 per cent or lower (Sahli). These did not belong predominantly to any one of the three categories. When hemoglobins of 70 per cent and over were considered, however, it was found that 82 per cent of the spontaneous group, 79 per cent of the drug-induced, and 72 per cent of the mechanically induced group showed this finding.

The white blood count showed significant differences according to the history given by the patient. Fifty per cent of counts on patients admitting mechanical induction showed a leucocytosis of 12,000 or more, with 80 per cent or more polymorphonuclears. Twenty-seven per cent of counts on the spontaneous group and only 17 per cent of those on the drug-induced group presented this finding.

It is now generally recognized that syphilis does not play the prominent role that was once attributed to it in the etiology of spontaneous abortion. In this series, 4 per cent of routine Wassermann tests were found to be strongly positive and 1 per cent doubtful. Drane[8] and DePuy[9] report similar frequencies. Only 1 per cent of the mechanically induced group had positive Wassermanns, while 5 per cent of each of the other two groups gave this evidence of syphilitic infection.

Much importance has been attributed to the cervical culture as indicative of interference or non-interference. *Staphylococcus aureus* has been considered proof positive of unskilled manipulation, and *Streptococcus hemolyticus* indicative of unclean instrumentation. No strong evidence for these views could be found in the present study. The former organism was found in 46 cultures distributed proportionately through all groups classified according to history of type of abortion. Only two of the 46 had temperatures of 103° F. or above. Both admitted mechanical induction. One of these died of subacute bacterial endocarditis, the blood culture being positive for *Streptococcus viridans.* Streptococci appeared in only 6 cervical cultures. Of the 3 cases in which viridans were found, 2 denied induction. One of these had an afebrile course, the other a moderate febrile reaction (100.4° to 102.8° F.). The third, who admitted drug induction, had a temperature of 103° F. None was fatal. The three cultures which were positive for hemolytic streptococci all occurred in the group who gave a history of drug induction. Two were afebrile; one had a temperature below 102.8° F. All made uneventful recoveries. The other positive cultures reported were: 11 colon bacilli, 10 diphtheroids, and 1 gonococcus. These were not associated significantly with either of the induced nor with the spontaneous group. None of the patients harboring these organisms were seriously ill. Studdiford has pointed out earlier that many of the strains of bacteria present in the vagina are avirulent.[6] We had no facilities for the routine culture of anaerobes. These were found in 92 per cent of cases showing positive cultures in Brown and Hunt's series.[10]

The fact that cervical culture gave little positive help in prognosis in this series should not lead to the conclusion that it is of no value. The negative finding is of considerable significance. Although no case of virulent hemolytic streptococcus infection happened to appear among the 502 cases reported here, since the completion of this study two have been seen who were so infected. It is felt that these patients owe their lives to the prompt recognition of the nature of the infecting organism (within twenty-four hours after admission) and the consequent prompt institution of appropriate therapy (sulfanilamide followed by curettage).

The management of these cases and the criteria for selecting those suitable for curettage have been described by Studdiford.[6] The proportion of the mechanically induced group curetted (59 per cent) was substantially below that of the drug-induced (68 per cent) and the spontaneous (71 per cent).

The 13 febrile patients who admitted mechanical induction and who were curetted spent an average of 13.4 days in the hospital, while the

15 febrile drug-induced and subsequently curetted patients required but 8.5 days' hospitalization per patient, and the corresponding group who claimed spontaneous abortion remained only 6.7 days in the ward.

In every group except the mechanically induced, curetted afebrile patients were in condition to leave the ward earlier than those treated conservatively. This difference could be observed most strikingly in the drug-induced group (5.6 and 8.5 days, respectively). The reason for the exception in the mechanically induced group was that the 18 patients treated palliatively had, for the most part, such mild symptomatology that they were discharged the day following admission. Two refused examination and left the hospital immediately against advice and two were moribund on admission and died in a few hours.

The gross mortality for the entire series was 0.9 per cent (5 deaths). The operative mortality was 0.6 per cent. Four of the patients who died admitted mechanical induction. Two of these confessions were terminal after repeated denial. One patient steadfastly denied both pregnancy and induction and, indeed, no evidence of pregnancy was found at autopsy. No satisfactory explanation of her illness and death was arrived at, but since autopsy revealed peritonitis and acute nephritis and lead was demonstrated in her liver, the suspicion arose that death might have been caused by mistaken efforts to interrupt a non-existent pregnancy. If the latter controversial case is omitted, there was no mortality in 450 drug-induced and spontaneous abortions, while that in 52 mechanically induced, was 8 per cent.

SUMMARY

1. To differentiate abortion from other pelvic conditions is not always easy. Thirteen per cent of this series were erroneously diagnosed on admission. Without curettage, probably half of these errors in diagnosis would have remained unrectified.

2. To differentiate induced from spontaneous abortion is often impossible. No effort should be spared, however, in the attempt to learn the circumstances surrounding the interruption of pregnancy, since these have the greatest significance for prognosis. In this series the mortality in 10 cases admitting induction by a midwife was 30 per cent; in 13 cases induced by a physician it was 7.7 per cent; in 478 cases claiming self-induction or spontaneous abortion it was nil.

3. "Drug-induced" seems to be practically synonymous with spontaneous abortion, by every criterion except the purely psychologic. The two groups correspond closely in laboratory findings, clinical course, and outcome.

4. Thirty-three per cent of previously gravid patients who claimed to have had spontaneous abortions at this time gave a history of previous spontaneous abortion. Only 5 per cent of the comparable group who admitted mechanical induction gave such a history.

5. Induced abortion has been said to favor spontaneous abortion in subsequent pregnancies. In this series only 5 per cent of patients who claimed that the present abortion was spontaneous gave a history of past induction.

6. Spontaneous abortion was no more frequent in first pregnancies than in those of higher order. Induced abortion increased with order of pregnancy. That is, the probability of an abortion being induced, all things being equal, increases with the number of pregnancies the woman has previously undergone. This does not apply to pregnancies of very high order (10 or more). Of these there were too few in the present series to furnish a basis for conclusion.

7. Low sedimentation rate, fever, leucocytosis and acute inflammation of the decidua and chorion were found to be more frequently associated with mechanically induced abortion than with drug-induced or spontaneous. These evidences of infection were, however, by no means confined to the former group.

8. The Wassermann test was positive in 5 per cent of drug-induced and of spontaneous, in only 1 per cent of mechanically induced abortions.

9. Low hemoglobin determinations were not significantly more frequent in any one category than in the others.

10. Bacteriology showed little correlation with history in this series. The fact that here cervical culture cast scant light on differential diagnosis or prognosis should not lead to the conclusion that it is of no value. Infection with the virulent hemolytic streptococcus is relatively rare (it did not appear in this series), but its prompt recognition is of vital importance.

11. Curettage was performed in 59 per cent of the mechanically induced group, 68 per cent of the drug-induced, and 71 per cent of those claiming spontaneous abortion. Operative mortality was 0.6 per cent. Average stay in the hospital of curetted patients was five to seven days.

The author wishes to express her deep appreciation to Dr. William E. Studdiford for the photomicrographs illustrating this paper and for his interest and encouragement without which this study would not have been possible.

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Leo Loeb as the first showed that the uterus, if traumatized while under the influence of an active corpus luteum, responds by the formation of structure not unlike the maternal portion of the placenta. This growth may become quite large and assume the appearance of a decidual tumor.

Investigations by the writers demonstrated that uteri of postpubertal ovariectomized rats treated with daily doses of 100 gamma of estradiol, 3 mg. of testosterone, or 3 mg. of pregninolon are sensitized to local trauma in such a manner that gelatinous tumors of the endometrial mole type develop at the site of injury. These observations give further support to the concept that both local injury and an appropriately prepared humoral medium are essential for tumor production.

Hugo Ehrenfest.

PRIMARY SIGNET-RING CELL CARCINOMA OF THE OVARY

With a Case Report

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WHEN Krukenberg in 1896 published his paper on five ovarian tumors which Marchand had offered to him for investigation and publication, he gave an accurate description both of the macroscopic and microscopic appearance of the new tumor but presented a deficient histogenetic explanation and a tentative and inaccurate definition. He suggested the term fibrosarcoma ovarii mucocellulare carcinomatodes. The consequence was that some of the various investigators who found and studied similar tumors after Krukenberg tended to do one of two things: Either they included cases which more or less differed from Krukenberg's material and therefore called them atypical Krukenberg tumors, or they enlarged the field of Krukenberg's entity. Unfortunately, different authors pursued different courses. The result is that at the present time, almost forty-five years after Krukenberg's original paper, we still lack a general and universally accepted conception of this tumor among gynecologists and pathologists.

Referring to Krukenberg's first suggestion of *fibrosarcoma ovarii mucocellulare carcinomatodes*, the outcome of all investigations carried out since Krukenberg's has proved that there is neither a fibroma nor a sarcoma present, that the mucinous cells are not specific, and that the carcinoma is a secondary one. To avoid committing themselves, many authors used the term "Krukenberg's tumor" without accurately explaining what they meant by this term. Prominent experts such as Frankl have expressed their dislike for the term "Krukenberg tumor" which is in agreement with the modern trend in nomenclature to avoid eponyms. The name Frankl suggested, which appears to be the most appropriate and accurate, is simply "metastatic carcinoma of the ovary" or eventually, "Krukenberg's metastatic carcinoma of the ovary." This latter expression implies a certain contradiction since Krukenberg himself doubted the carcinomatous character of the tumor and knew nothing of its metastatic origin. Schlagenhaufer was the first to show that most Krukenberg tumors originated from an intestinal primary tumor growth; however, he still believed that the more rare true Krukenberg was primary in the ovary, but that it was frequently duplicated by a more common similar tumor which was a metastasis.

Not until done by Wagner, Cohn, Rosinski, and others was it definitely established that the overwhelming majority of these tumors are typically bilateral ovarian metastases of primary carcinomas of an intestinal

mucous membrane, most frequently of the stomach. This genetic definition is now generally accepted. The tumor usually produces a smooth, firm, uniform eccentric enlargement of both ovaries. It has a variegated cut surface due to frequent areas of microcystic changes and areas of intracellular mucinous secretion amid more solid areas of a fibrous type of tissue. Histologically the tumor is characterized by small cysts of mucin-producing epithelium and solid small clusters of similar columnar epithelial cells which as single cells invade the ovarian stroma diffusely and in large numbers. The stroma shows a reactive proliferation which misled Krukenberg and other investigators to describe a fibromatous or sarcomatous component.

Krukenberg described the signet-ring cells as specific for his tumor but already Marchand pointed out that such cells can be found not too rarely in the floor of mucin-producing adenocarcinomas, wherever they originate. One of us (W. S.) explained the transformation of mucin-producing columnar cells into signet-ring cells as a result of retained potency for secretion combined with a loss of polarity due to the embedding of the isolated tumor cells in the apolar stroma. We now know with certainty that signet-ring cells can be found with all mucin-producing carcinomas and even with chronic inflammation of mucin-producing mucous membranes, such as the uterine cervix or the pelvis of the kidney. We admit that signet-ring cells are characteristic but not specific for so-called Krukenberg tumors.

The above definition describes Krukenberg's tumor as an ovarian metastasis for which, in the overwhelming majority of cases, a primary tumor can be proved in the intestinal tract, either by clinical investigation or autopsy. Still, supporting Krukenberg's original conception, a few cases have been published which because of their histologic structure were classified as Krukenberg tumors without demonstration of a primary tumor. Such cases were called "*primary Krukenberg tumors.*" In this group only those cases can be correctly accepted in which the absence of a primary tumor was proved by autopsy or by the clinical observation that the patient was found well several years after simple extirpation of the ovarian tumor, which would have been impossible with an intestinal primary.

Cases of so-called primary Krukenberg tumors have been published by Glockner, Schenk, Marchand, Miner, Kruger, Frankl, and recently by Greenhill and Andrews.

Ewing, who himself has seen five cases of Krukenberg tumor and one primary carcinoma of the ovary with myxomatous changes, believes that true Krukenberg tumors are always secondary. He further believes that "primary carcinomas presenting this structure regularly yield areas of a different type." Masson interprets this concept as although "small portions of certain alveolar carcinomas of the ovary present the typical picture of Krukenberg tumors, there is little, if any, suggestion of glandular arrangement of cells in a true Krukenberg tumor." Masson's statement would reduce the field of true Krukenberg tumors considerably, for there are many cases which

present the combination of adenomatous structures with infiltrating signet-ring cells in varying proportions.

The common feature of all the case histories of "primary Krukenberg tumors" is the similarity of the histologic picture with the definitely established secondary carcinomas. On the other hand, and this should be emphasized, these tumors are definitely different from ovarian carcinomas which develop by malignant degeneration of pseudomucinous cystomas. The characteristic feature of the latter group is the presence of large cystic cavities separated by paper-thin septa, lined with a high columnar mucin-producing epithelium, and filled with thick mucinous contents. It is characteristic of these tumors that the stroma is in the background, and constitutes only a small part of the parenchyma; whereas, the overwhelming part of the tissue is represented by the epithelial cells and their product—mucin. It is characteristic of the secondary, as well as the primary, Krukenberg tumor that the stroma forms a great portion of the tumor. In fact the proliferation of stroma goes so far as to make the erroneous diagnosis of fibroma or sarcoma possible. The epithelial-lined cavities of Krukenberg tumors remain very small and their diameter barely reaches gross visibility. In spite of the most dense infiltration by signet-ring cells, the greater part of the tissue is still formed by the stroma.

The problem of the so-called primary Krukenberg tumor can be formulated as a question whether or not there is a possibility for the ovary to produce such a tumor from itself or by itself. As long as two or three observations were published, doubts as to whether these isolated observations are not due to incomplete search for a primary tumor seemed to be justified.

Since the number of well-established observations have increased to nine authentic and two doubtful cases, it seems justified to accept the statement that the ovary by itself can produce tumors (a) which morphologically duplicate the secondary metastases (b) of primary intestinal carcinomas. This manner of expressing these observations appears to be clearer than to speak of the existence of two types of Krukenberg tumors: The rare primary Krukenberg tumor (a above), and the more common secondary Krukenberg tumor (b above). We have had the opportunity of investigating one case which may be added to Group a.

CASE REPORT

A 61-year-old, obese, white female was admitted to the medical service of the Cook County Hospital, complaining of severe generalized abdominal pain. Thirty years ago she experienced her first acute attack of right upper quadrant pain. Ten months prior to admission she noted an increase in the intensity of the pain and a tendency for it to become generalized. For the past four months the pain was described as being continuous from morning until night, most severe over both right upper and lower quadrants. For the two weeks preceding admission she ate only soup, milk, water, and occasionally an egg, because of an anorexia. She further noted a progressively enlargening abdomen in recent weeks.

Physical examination revealed an extremely obese white female with a tensely distended abdomen, dyspnea, wheezing, and she complained of generalized abdominal

pain. Pulse was 88; respirations, 39 per minute; temperature, 99.2° F.; blood pressure, 136/90. The heart and lungs were normal except for the rapid respiratory rate and limited respiratory excursion. A ballotable mass was palpated in both upper quadrants which extended below the umbilicus on the right side. There was no tenderness or rigidity and bowel sounds were audible. A fluid wave could not be elicited. Pelvic examination was essentially negative. The extremities showed no edema and the reflexes were physiologic.

Examination of the blood revealed a hemoglobin of 58 per cent (Sahli), 3,720,000 red blood cells, and 13,950 white blood cells per cubic millimeter. A blood smear contained 84 per cent polymorphonuclear leucocytes, 10 per cent lymphocytes, and 6 per cent monocytes. The icterus index was 7. Nonprotein nitrogen was 39 mg. per cent and the creatinine was 1.6 mg. per cent. Blood diastase was reported as 16 units. The Wassermann test was negative. The urine was negative for albumin

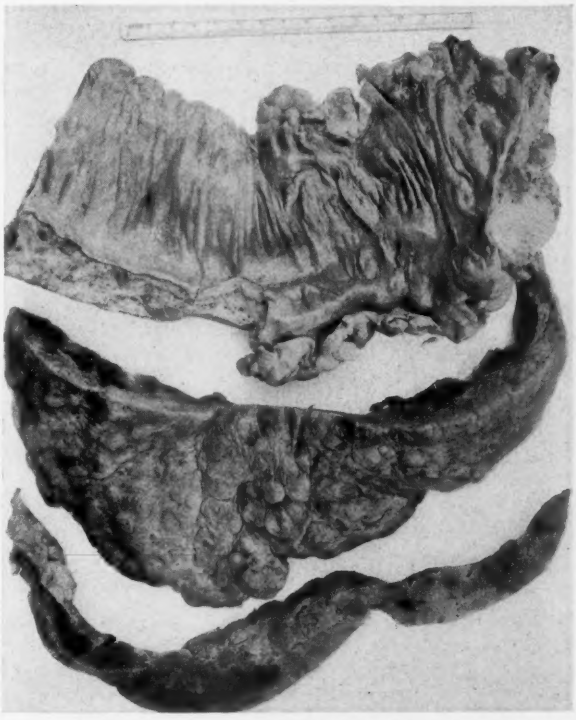

Fig. 1.—Transverse colon with omentum, the latter thickened by the infiltrating tumor tissue. To show the thickness of the omentum a slice is cut out and placed beneath.

and sugar. The Graham-Cole test failed to visualize the gall bladder, and a flat plate of the abdomen revealed a marked hypertrophic arthritis of the spine and a peripheral displacement of the colon. An electrocardiogram showed a left axis deviation and myocardial damage as suggested by a flattening of the T-waves in all leads.

On the fourth day following admission a paracentesis was performed and approximately 5,000 c.c. of a hemorrhagic ascitic fluid was withdrawn from the abdomen. Three days later the patient developed symptoms of intestinal obstruction and vomiting which was overcome with nasal catheter suction siphonage and parenteral fluids. The patient grew progressively weaker and died on the fifteenth day of her stay in the hospital.

Autopsy Findings.—(Dr. J. D. Kirshbaum.) A layer of abdominal subcutaneous fat 68 mm. in thickness was present. The abdominal cavity contained over 3,000 c.c. of a hemorrhagic ascitic fluid. The omentum was transformed into a firm plaque of

tumor tissue filling both upper quadrants and extending down as far as about the level of the umbilicus. This plaque averaged 3 cm. in thickness and evidently was the ballotable mass palpated on abdominal examination. The mesentery of the transverse colon was transformed into another plaque of tumor tissue of similar thickness (Fig. 1). Numerous small tumor nodules studded the serosal surfaces of the small intestines and the pleural and peritoneal surfaces of the diaphragm. The peritoneum of the anterior abdominal wall and of the pelvis appeared to be free. The heart presented parenchymatous degeneration of the myocardium, and the lungs showed edema and passive congestion of all the pulmonary lobes. The pleura on the diaphragmatic surface of the right lower pulmonary lobe contained numerous small tumor deposits.

The gall bladder showed a marked hydrops. It measured 12 by 7.5 by 5 cm., and contained about 250 c.c. of a dirty grayish green inspissated material. The wall of the gall bladder was thickened up to 3 mm. and composed of grayish white material of firm consistency. Numerous pinhead to 3 mm. in diameter dark concretions were floating free in the gall bladder contents, but a 22 by 18 by 13 mm. concretion was impacted in the neck of the gall bladder. The mucosa of the gall bladder was smooth and glistening. The cystic duct showed an atresia at its

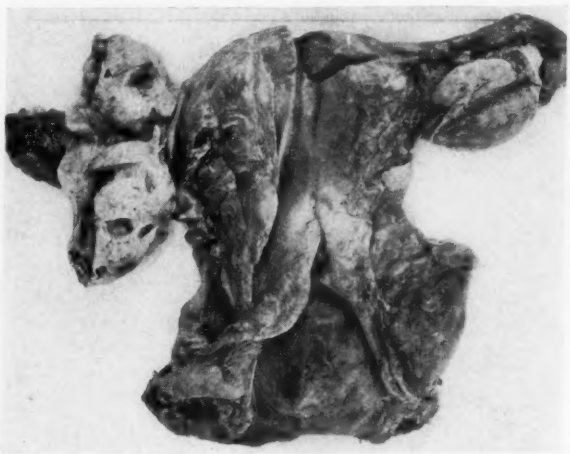

Fig. 2.—Uterus, tubes, and ovaries. The right ovary presents the primary carcinoma.

opening into the ampulla of the gall bladder which on careful microscopic examination showed chronic inflammatory changes without any evidences of tumor cells. The common bile duct was elongated and dilated but its lumen was free as were all the other extrahepatic bile ducts. By gross examination there was no evidence of carcinoma in the biliary tract.

The kidneys and the liver showed evidences of passive congestion. The spleen contained an ancient infarct.

The right ovary measured 5 by 4 by 3.5 cm. and contained several thin-walled cysts which projected above the surface. On cross section the ovary consisted of firm trabeculated yellowish-white tissue interspersed throughout by cystic cavities, from 2 to 20 mm. in diameter, filled with a mucoid material. The left ovary measured 4 by 1.3 by 1 cm. and on cross section was yellowish white and fibrotic; on gross inspection, it was apparently uninvolved by tumor tissue. The uterus was of normal size but beneath the perimetrium of the anterior fundic wall several up to 1 mm. tumor nodes were found (Fig. 2). The peritoneum of the vesicovaginal and rectovaginal septa contained plaques of tumor tissue.

The mucosa of the stomach was dark reddish brown in color, the folds and rugae were flattened, and the mucosa was smooth throughout. Its serosal surface was

studded by pinhead size tumor nodules. A single 5 mm. nodular peritoneal deposit protruded above the mucosal surface of the jejunum without ulcerating through it. The mucosal surface of the esophagus and duodenum was everywhere smooth. The mucosa of the ileum was smooth as was the mucosa of the large intestine. The pancreas and its ducts presented no changes.

An accurate detailed examination of the stomach, small and large intestines, gall bladder and bile ducts, and the pancreas and its ducts gave no evidence of a malignancy.

Microscopic Findings.—The right ovary (site of the tumor) was composed of a loose and partially edematous stroma which contained numerous irregularly shaped small cavities which were lined by low columnar epithelium, containing a pale staining granular cytoplasm. With the mucicarmine stain the cytoplasm of the epithelial cells presented red-staining mucin droplets, proving the mucinous char-

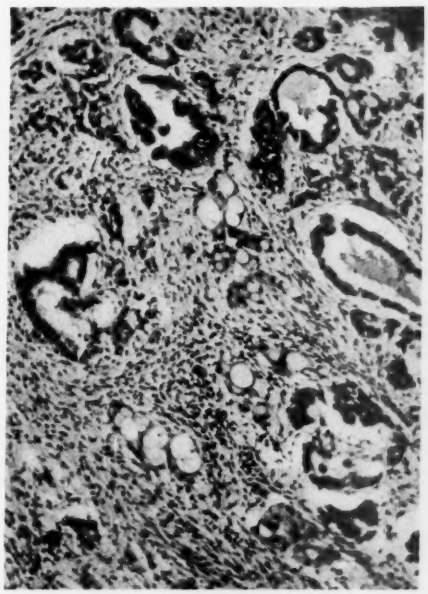

Fig. 3.

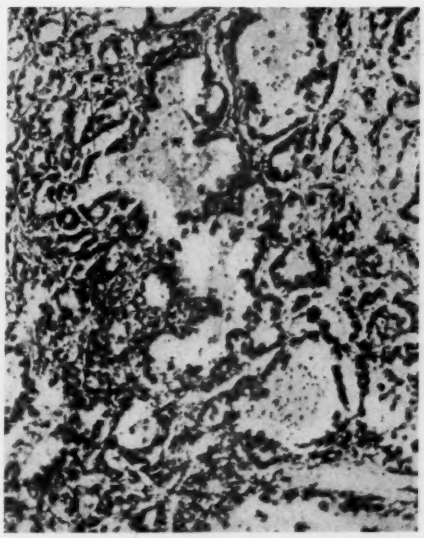

Fig. 4.

Fig. 3.—Right ovary; cystic and papillomatous tumor tissue, groups of typical signet-ring cells.

Fig. 4.—Right ovary, primary tumor presenting a labyrinth of small cystic cavities, lined with cuboidal or low columnar epithelium which forms low papillary projections.

acter of the cell. In many areas the epithelium of the cyst wall became many cell layers in thickness, the nuclei showed irregularities in size and shape, and the epithelial cells invaded and infiltrated the surrounding stroma as solidified glands, acinar formations, groups of cells, and as single cells. Many of the single cells and cells of the small groups were transformed into typical signet-ring cells with a drop of mucin in the center (Fig. 3). Many cysts contained epithelial cells floating freely within the mucinous contents of the cyst; these frequently were of the signet-ring appearance. In other sections of the ovary, small cysts, up to 15 mm. in diameter, were seen to be surrounded by a dense layer of fibrillar connective tissue which was invaded by epithelial downgrowths from the epithelium lining the cyst. With the mucicarmine stain it was shown that all the cysts were filled with large quantities of partially retracted mucin (Fig. 4).

The left ovary showed a marked fibrosis of the stroma which contained a few corpora candicantia. The albuginea in one area contained a few surface epithelium

inclusion cysts which were lined by a low cuboidal epithelium and filled with a seromucinous fluid, and surrounded by a dense frame of collagenic fibrils. No evidence of tumor tissue was seen.

Slides of the anterior fundic wall of the uterus revealed the myometrium to be markedly fibrotic and the demarcation line between endometrium and myometrium was jagged. A marked increase in perivascular connective tissue was present around the larger blood vessels. Beneath the serosa cystic and solid deposits of the carcinoma could be seen to invade the superficial layer of the myometrium (Fig. 5). In some of the cystic deposits many epithelial cells contained droplets of secretion, thus gradually transforming themselves into signet-ring cells. In between the tumor aggregates old blood pigment within histiocytes could be seen.

Sections of the omentum (Fig. 6) showed large areas of fat separated by dense vascular connective tissue septa. These septa were riddled by large and small cysts, glandular structures, small solid acini, and even single cells of a low columnar epithelium. These cells, especially those lining the larger cystic cavities, produced

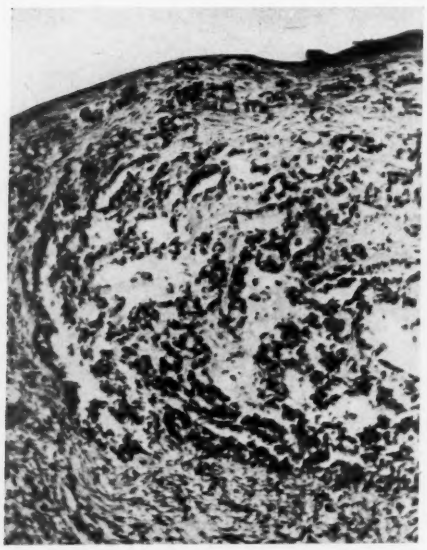

Fig. 5.

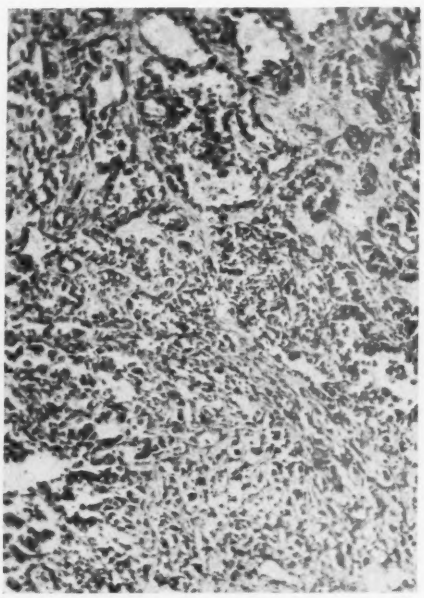

Fig. 6.

Fig. 5.—Deposits in the myometrium beneath serosa of uterine fundus.
Fig. 6.—Deposits in the omentum.

large quantities of a thick mucin. Some of the single isolated cells were transformed into classical signet-ring cells by the production of a central intraprotoplasmic drop of mucin. Small interstitial hemorrhages were occasionally seen within the field of carcinomatous deposits.

Several sections of transverse colon and its adjoining mesentery revealed an extensive replacement and separation of muscle cells by tumor deposits which were continuous with similar tumor masses within the mesentery. The mucosa was everywhere intact and uninvaded. The tumor deposits in some areas were cystic, in others glandular, and in still other areas infiltrating as solid clusters or single tumor cells. The cells everywhere showed an abundant mucin-staining cytoplasm, and in the case of the isolated cells, were frequently of the signet-ring shape. Within the mesentery itself the tumor aggregates were separated by very thick layers of edematous connective tissue.

A section of jejunum through the subserosal tumor nodule revealed a tumor deposit identical to that which has already been described but not invading the intact mucosa.

Sections of the gall bladder revealed a much thickened wall, largely replaced by dense fibrous tissue with frequent areas of hyaline degeneration. No tumor cells were seen.

Sections of the liver showed changes compatible with severe parenchymatous degeneration and passive congestion. No tumor deposits were seen within the liver.

DISCUSSION

The tumor in the ovary where it infiltrates the stroma by small groups and by single cells duplicates the so-called Krukenberg structure. The small cystic cavities, too, as far as they are round or slightly oval, fit into the picture of a Krukenberg tumor. They are frequently found combined with infiltrating signet-ring cells in ovarian deposits of primary intestinal carcinomas. Microscopic size cystic cavities, composing by themselves alone large ovarian tumors, have been described by Pfannenstiel as an entity and called "parvilocular cystoma." However, it is possible that this tumor of Pfannenstiel's is not an entity within itself but a special subgroup of the Krukenberg tumor. There is a close relationship between certain areas of some Krukenberg tumors in which the tumor forms microscopic small cysts, and the tumor which was described by Pfannenstiel. The tumor described by Pfannenstiel is very rare and since publication of his first cases in 1908 only a few more have been added to the literature.

In our case, in some areas the lining epithelium of the small cystic cavities shows adenopapillary projections which are not found in the typical Krukenberg tumor. These findings would tend to place the tumor into a relationship with the adenopapillary pseudomucinous cystoma. However the latter tumor has larger cavities, thinner septa, produces more mucin, and its cells have very little tendency to change into signet-ring cells; neither in the benign form when they float free in the mucinous secretions of the cysts, nor in the malignant form when they do the same or when they invade the stroma.

The subperitoneal deposits similarly duplicate by their adenopapillary projections the adenopapillary pseudomucinous cystoma, and by their tendency for signet-ring cells, the Krukenberg tumor. It has to be admitted that the presence of signet-ring cells in the subperitoneal metastases is less characteristic here of Krukenberg tumors than their presence in the ovary.

The unilateral development of this tumor, the small size, and the rather moderate increase in interstitial connective tissue, too, differ from the picture of a typical Krukenberg tumor, as well as the progressive peritoneal involvement which is found in only a few typical Krukenberg tumors. In the majority of cases the peritoneum is free and the propagation of the tumor from the primary site to the ovary does not occur by gravity through the peritoneal cavity, but as Jarcho and others have emphasized, by retrogressive lymphatic flow. On the other hand, direct proof cannot be given that the tumor originates from the ovary;

only by exclusion, since accurate gross and microscopic examination eliminated any other primary focus. The interpretation of this tumor as a primary endothelioma of the peritoneum, in the manner of explanations used for similar cases twenty to thirty years ago, is not in accordance with our modern conception of endotheliomas. Papillary projections and mucin production are characteristics which we do not like to attribute to peritoneal endothelium or its neoplasms. At least the origin of such tumors from the peritoneum has never been proved, although, for example, in ectopic pregnancies the peritoneum of the Fallopian tube and broad ligament may produce papillary projections of high columnar cells and a sort of mucoid secretion.

Concerning the origin of primary Krukenberg tumors, Novak and Gray have suggested tracing them back to teratoid inclusions. This seems likely, and we may be successful some day in finding a case of primary Krukenberg tumor which still shows the residue of teratoid tissue. Our case shows by its adenopapillary structures a certain relationship with the pseudomucinous cystoma; by its infiltrating signet-ring cells a close relationship to the Krukenberg tumor. However, since Robert Meyer has definitely proved that some pseudomucinous cystomas develop from the intestinal portion of teratoid ovarian inclusions, there is a possibility of linking a primary Krukenberg tumor like ours with the pseudomucinous cystoma of teratoid origin.

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The author reports on the use of placental blood, stored up to fifteen days, in 220 transfusions. Blood from 5 to 6 placentas was used for each transfusion. Reactions, all mild, were observed in 5 per cent but were no more frequent than with fresh adult blood. The only chemical change of importance due to storing of blood was glycolysis increasing from day to day. There is a complete disappearance of granulocytes after the seventh day. The total white blood count decreases by the fifteenth day to 4,000-5,000 per c.mm. The erythrocytes are in general well preserved, and their power to combine oxygen is maintained. Slight hemolysis appears after several days of storing but almost never amounted to more than 1 per cent up to the tenth day. Quantities of free hemoglobin up to 710 mg. per 100 cm. (5 per cent hemolysis) do not seem to produce any undesirable effect.

Carl P. Huber.

A STUDY OF PELVIC MEASUREMENTS IN 550 SOUTHERN WOMEN

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MENGERT[1] reported recently that the average pelvic measurements of 4,144 Iowa women agreed closely with those given by Williams.[2] For a long time we have had the clinical impression that the measurements for women in this area were much smaller than those given in textbooks,[2] and this apparent difference in size stimulated us to study the average pelvic measurements in a series of southern women.

In the past few years many changes have taken place in the conception of the shape of the average normal pelvis. Greulich and Thoms[3] found that only 31.9 per cent of adults had the type of pelvis (gynecoid) which, according to anthropologic literature, is proper for white women. A comparison of the average measurements of the women of our series with those of Iowa led us to believe that some revision of the concept of size and measurements which are considered to be normal for the female pelvis should be made. We feel that measurements which would be normal for one group in the United States are not necessarily typical and normal for the average pelvis in another section of the country.

Five hundred and fifty women from the Touro Infirmary Clinic and the Touro-Tulane Clinic who were delivered between January, 1939, and January, 1940, were studied as to measurements and weights at term, type of delivery, and size of the baby. The average measurements were as follows: interspinous 23 cm., intercrestal 26 cm., external conjugate 18.5 cm., biischial or transverse outlet 7.9 cm., and 44 per cent of the diagonal conjugates could be reached. Each of these external measurements is 2 to 3 cm. smaller than those of Williams' series (see chart), and with the exception of the biischial is 2 to 3 cm. smaller than the Iowa women. Mengert found the average transverse of the outlet to be 9.3 cm., while the average for women in this area is 7.9 cm.

TABLE I

	TOURO	WILLIAMS	IOWA
Interspinous	23.0	25	25.5
Intercristal	26.0	28	28.0
External conjugate	18.5	21	19.6
Diagonal conjugate	44% reached		22% reached
Biischial or transverse outlet	8.0 (7.96)	10.5	9.3

The method followed in this study was as follows: On the initial visit to the clinic the measurements were taken by the intern and checked by the resident. The transverse of the outlet and diagonal conjugate

were then checked by a staff member. When the patient had reached the eighth month, the measurements were checked again by the resident and the staff member, with special attention to the diagonal conjugate and transverse of the outlet. Thus in most cases the diagonal conjugate and transverse of the outlet were checked six times before the patient was delivered. We feel that the measurements are dependable and accurate to 0.5 cm. To check further the impression that pelves of southern women are small and to check the accuracy of our measurements, we measured a small number of pelves used by the students in anatomy. These pelves come from indigent patients of this area and should be representative. A few x-ray plates were also checked and found to be in line with the clinical measurements.

RESULTS

The External Conjugate.—The external conjugate or Baudeloque's diameter was found to be 18.5 cm. In Williams' series[2] this figure was 21 cm. and in Mengert's series[1] 19.6 cm. Williams[2] states that "an external conjugate of 18 to 19 cm. is a danger signal" of contracted internal diameters. This could not hold in this series, since 18.5 cm. is our average, and since 72 women (13 per cent) had an external conjugate of 17 cm. or less and had no internal contraction.

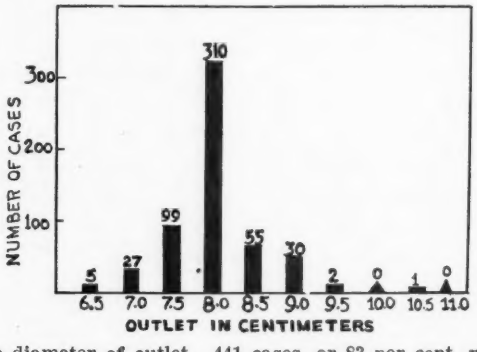

Fig. 1.—Transverse diameter of outlet. 441 cases, or 83 per cent, were 8 cm. or less; 32 cases, or 6 per cent, were 7 cm. or less, considered as contracted outlet.

The Transverse of the Outlet.—The normal biischial diameter or transverse of the outlet is given by Williams[2] as 10.5 to 11.0 cm. Not a single transverse of the outlet of 11.0 cm. was seen in this clinic in the past year. Only one woman had a transverse of the outlet of more than 9.5 cm.; 30 women had a transverse of the outlet of 9 cm., in 55 women it measured 8.5 cm., in 310 (or 60 per cent) 8 cm., in 99, 7.5 cm., in 27, 7 cm., and 5 negroes had a transverse of the outlet of 6.5 cm. or less (Table II). No white woman had a transverse of the outlet of less than 7 cm. Williams states that "whenever the transverse diameter of the outlet measures 8 cm. or less we designate the pelvis as funnel" and he noted 6 per cent of funnel pelves in 10,000 cases. On this basis our incidence of "funnel pelvis" would be 83 per cent, or 441 cases out of 529. It is a common observation that outlet dystocia is very rare, and we agree with this. We have had no difficulty with outlets of 7.5 cm. of which we had 99 in this series. A patient with an outlet of 7 cm. requires careful watching and a larger episiotomy to avoid damage to the perineum and rectum, but we have seen no true dystocia result. The posterior sagittal should always be measured in these cases. We feel that a transverse of the outlet of 8 cm. should not be the standard for a funnel pelvis in southern women, but that 7 cm. should be considered borderline and 6.5 cm. or less should indicate a true funnel pelvis for women in this area. Using these standards our incidence of funnel pelvis is 6 per

cent (see Fig. 1). (Note: We do not routinely measure the anterior posterior diameter of the outlet and posterior sagittal, so these figures were not submitted to analysis. The posterior sagittal, as noted above, is measured when the biischial is 7.5 cm. or less.)

The Diagonal Conjugate.—The majority of women came to the clinic in early pregnancy and the pelvic measurements were checked then, as well as at the eighth month, at which time special effort was made to reach the diagonal conjugate measurement. In 44 per cent the promontory could be reached as against 22 per cent in Mengert's series which is again in line with evidence that the pelves of southern women are smaller than those of women in other areas (Figs. 2 and 3).

More concrete evidence of the small size of the pelves of southern women can be deduced from the x-ray studies of Torpin and Holmes[4] of the University of Georgia. They measured the inlet of 400 women, divided the pelvic types into 4 groups, and then showed the number of cases in each group with different lengths of conjugate vera. We find that if we add from 1.5 cm. to 2 cm. to each conjugate vera we have the approximate diagonal conjugate in their series. Torpin's and Holmes'

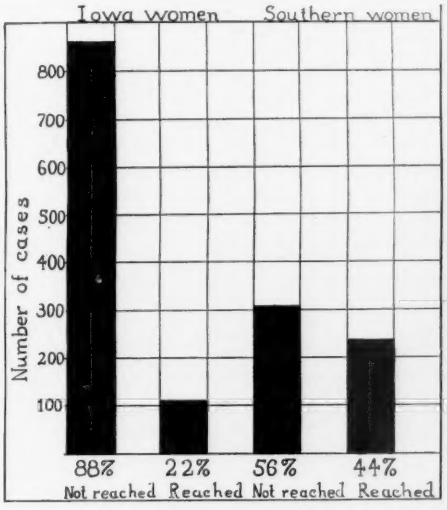

Fig. 2.

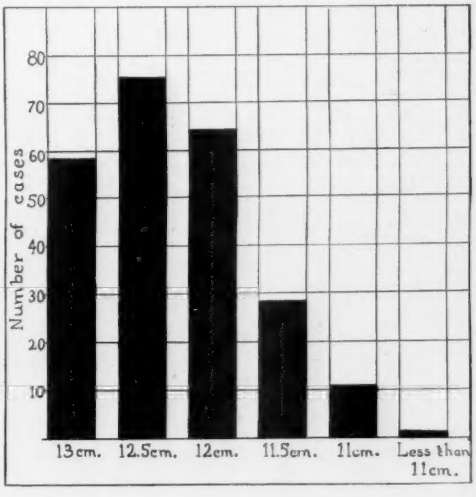

Fig. 3.

Fig. 2.—Sacral promontory not reached in 88 per cent of Iowa women. Sacral promontory not reached in only 56 per cent of southern women.

Fig. 3.—Slightly less than half (44 per cent) of the diagonal conjugates could be reached. One hundred and ninety-eight of the 240 diagonal conjugates reached measured between 12 and 13 cm.

findings agree with our clinical determinations, as 88 per cent of their diagonal conjugates would be 13 cm. or less, and 60 per cent to 70 per cent of these could probably be measured clinically. Only 12 per cent of diagonal conjugates in their series were more than 13 cm. as obtained by addition of 2 cm. to x-ray conjugate vera (Table II).

TABLE II

	CONJUGATE VERA IN CM. MEASURED BY TORPIN					
	6-8.5 cm.	9 cm.	10 cm.	11 cm.	12 cm.	13 cm.
Converted to diagonal conjugate (2 cm. added)	10.5 cm. or less	11 cm.	12 cm.	13 cm.	14 cm.	15 cm.
Cases total 400	6	36	148	163	39	8

88 per cent had a diagonal conjugate of 13 cm. or less, and 60 per cent could probably be reached clinically.

RACIAL DIFFERENCES

Many statements have been made regarding racial differences in pelves, especially as regards white and colored patients. Some local physicians also expressed the belief that the reason for the apparent smallness of the female pelvis in New Orleans was because the majority of women came from Latin stock and were small in stature. So the clinic patients were divided into 3 groups for study as follows: 137 "Latins" made up of women of French, Spanish, and Italian descent; 170 "Anglo-Saxons" of English, Irish and German descent, and a third group of 238 negroes. As shown in Table IV the measurements of each group are surprisingly similar to the others. The measurements were practically identical for the diagonal conjugate, transverse outlet, and external conjugate diameters, while only the interspinous varied as much as 1 cm. from the general average (Table III).

TABLE III

	ANGLO-SAXON	LATIN	NEGROES	TOURO ALL GROUPS
Interspinous	23.24	24.2	22.3	23.0
Intercrestal	26.4	26.4	25.75	26.0
External conjugate	18.28	18.28	18.7	18.5
Diagonal conjugate	41%	40%	48%	44% reached
Biischial or transverse outlet	7.9	7.9	8.0	8.0 (7.96)

There is no marked difference in the size and shape of the negro pelvis and the pelvis of the southern white woman as is described by some northern writers.[5] Neither have we noticed the presence of rickets (or the contracted "rachitic pelvis") which is said to be common in the negroes living in the North.

This was mentioned by W. E. Levy,[6] in 1926, who compared 500 negro women and 500 white New Orleans women from an obstetric viewpoint. He included pelvic measurements as a part of his study and found "very little difference in the pelves of the two races except in two of the external measurements." His measurements were practically the same as those found in this study, varying no more than 0.4 cm., but he made no comparison of these figures with pelves of northern women.

The average weight for women of Anglo-Saxon descent was 143 pounds at term, for Latin women 144 pounds, and for negro women 146 pounds. The average weight of the whole group at term was 145 pounds. This is probably smaller than the average for women of Scandinavian descent at term, but we have no proof of this. The negroes weighed more at term because most of these patients in our clinic are multiparas and are from a higher age group, while the white women are more than 90 per cent primigravidas.

INCIDENCE OF CONTRACTED PELVIS

As stated above, 83 per cent of outlets were 8 cm. or less, and this would be the incidence of funnel pelvis according to Williams' standards. But taking 7 cm. or less as our standard for funnel pelvis, our incidence is 6 per cent. We had 27 patients with outlets of 7 cm. and all delivered

without difficulty with low forceps plus episiotomy which is routine in our clinic for primiparas. Five women (all negroes) had an outlet of 6.5 cm. or less. Two of these, with small babies, delivered from below. The other 3 with outlets of 6.5 cm., 6 cm. and 5.5 cm., respectively, were delivered by section, because the babies were rather large.

Fourteen women (2.6 per cent) had inlet contractions (Table III). Twelve had a diagonal conjugate of 11 cm. and 2 had a diagonal conjugate of 10.5 cm. Both women with diagonal conjugates of 10.5 cm. were delivered by section. One of these two also had an outlet of 6 cm. One patient with a diagonal conjugate of 11 cm. who had had two previous sections was delivered by cesarean section. One woman with diagonal conjugate of 11 cm. had a Porro section after a long difficult labor and Bandl's contraction ring (fetal death). Another patient with a diagonal conjugate of 11 cm. had a transverse arrest and was delivered of a 9-pound male by midforceps plus episiotomy, followed by shock from hemorrhage. The remaining 10 women with diagonal conjugates of 11 were delivered with comparative ease by low forceps and episiotomy. Three other women with apparently average measurements for our general group required cesarean section during the year; 2 for cephalopelvic disproportion and one for previous section. Twelve sections were done in a group of 550 women delivered from January, 1938, to January, 1939, for "all indications"; an incidence of 2.2 per cent. Eight of these sections were done for cephalopelvic disproportion, an incidence of 1.4 per cent. No versions were done and only 21 midforceps were done, an incidence of 3.8 per cent. There were 8 stillbirths during the year, an incidence of 1.4 per cent. Three of these fetal deaths, however, were due to prematurity so that the corrected mortality of term infants was 0.9 per cent.

TABLE IV

			SECTIONS	MIDFORCEPS	VERSION	BREECH EXTRACTION	LOW FORCEPS AND EPISIOTOMY	SPONTANEOUS
All cases		550	12	21	0	27	222	268
Contracted pelves	Inlet	14	3	1	0	0	10	0
	Inlet and outlet	1	1	0	0	0	0	0
	Outlet	31	2	0	0	0	29	0
		46						

There were two maternal deaths during the year; neither patient was operated upon. The first patient had pyelonephritis and delivered a premature infant precipitately without internal examination. She died in three weeks with a staphylococcal septicemia. The other patient, a negro, had tuberculosis and died in labor. Autopsy showed Pott's disease and a psoas major abscess.

If southern women have smaller pelves than northern women, the question of the relative size of the babies arises. Williams[2] gives 7½ pounds as the average weight of full-term babies. In our series we found the babies of Latin mothers to average 7.36 pounds, those of Anglo-Saxon 7.41 pounds, and the negro babies weighed 7.61 pounds. Most of the negro patients were multiparas; this accounts for the larger size of the babies in this series. The average of the whole group was 7.53 pounds which agrees with the figures given in most textbooks. Thus it appears that southern women deliver average-sized babies through pelves the minimum diameters of which are somewhat smaller than the measurements given in the majority of American textbooks.

SUMMARY AND CONCLUSIONS

1. We believe that the obstetrician should know what is the typical normal pelvis in his particular section of the country.

2. The average measurements in 550 southern women were found to be interspinous 23 cm., intercrestal 26 cm., external conjugate 18.5 cm., biischial 8 cm., and 44 per cent of diagonal conjugates could be reached.

3. Only an average transverse of the outlet of 7 cm. or less should be considered as diagnostic of funnel pelvis.

4. We are of the opinion that in the past many patients in this area have been subjected to cesarean section without a trial of labor because of a supposedly contracted pelvis when in reality the measurements were the average for women in this section.

5. Since a larger group of southern women have small pelves, our operative incidence and incidence of section could properly be higher than in some other locations. The figure is 1.4 per cent, which is not high, and the authors feel that more mistakes have been made in denying patients section than in being radical.

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A CLINICAL STUDY OF THE INCREASED RESPONSE OF THE FULL-TERM GRAVID UTERUS TO PITUITRIN AFTER ALKALINIZATION

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SCIENTISTS have theorized and rationalized from the earliest times concerning the causes of labor. Chemical and endocrine studies have been undertaken, both in animals and in man, and many probable predisposing factors for the normal onset of labor have been promulgated but nature still hides the secret of the exciting cause.

It does seem, at present, that a certain something develops in the blood which either brings on labor itself or so sensitizes the uterus that a substance, normally present, has an oxytocic effect. For instance, Jeffcoate[1] has shown that estrin is essential for all uterine contractions in vivo; and since, in its absence, coordinated contractions do not exist, it may be postulated that the presence of estrin is a necessary condition for labor. But this does not mean that estrin acts alone in the causation of labor. Its presence increases most remarkably about the fifth month of gestation and, although it rises gradually until term, there is no significant change at that time which would initiate the violent contractions of labor.

Beginning with Hippocrates, many obstetricians and midwives have noticed that certain changes in the weather may precipitate labor in groups of patients. Women themselves believe in the tradition that a storm might bring on the pains. DeLee refers to it. We have observed that births seem to occur in groups, with interval lulls, and were, therefore, led to a study of the influence of meteorologic events on labor pains. This work, unpublished, analyzed the occurrence of over 16,000 births in St. Louis in 1937 and showed that a preponderance were associated with the passage of cold air masses.

If meterologic stimulation of the organism is a fact and the onset of labor can be traced to changes in the meteorologic environment, other changes should be measureable in rhythmic shifts which coincide to changes in the weather chart.

Petersen,[2] in an extensive study, observed, in detail, changes in the blood pressure, serum proteins, blood pH, carbon dioxide-combining power, blood electrolytes, and basal metabolic rate which occur as a result of certain weather mixtures. He has shown that the passage of a cold air mass results in smooth muscle spasm and corresponds, in general, to sympathicotonia. His studies reveal an increased blood pH and carbon dioxide-combining power coinciding with these so-called cyclonic fronts of the weather.

Reasoning from the results of our study which showed an increased number of births during this type of weather, we believe that the increase in the body's alkalinity at this time could be considered as the necessary unknown quantity that conditioned the individual for labor.

In brief, it has been demonstrated, statistically, that the distinct periodicity in the precipitation of labor is to be related to the passage of a cold air mass and that this phase, besides manifesting itself in smooth muscle contractions, is a definitely alkaline phase.

ACID BASE BALANCE OF THE BLOOD DURING PREGNANCY

Examination of the literature on the subject of acid-base balance during pregnancy reveals a maze of confusing and contradictory observations.

Nice and others[3] and Oard and Peters[4] report a compensated alkali deficit while Meyers and Muntwyler[5] and Dieckmann and Wegner[6] show evidence which indicates that the change, if any, is toward the alkaline side. Unfortunately, we have no determinations, as far as I can find in the literature, taken in series, during the period that immediately precedes the onset of labor. I believe we would find an alkaline preponderance at this time, since labor is most commonly precipitated on the barometric highs and on the cold fronts when there is a greater tendency to spasm and relative blood alkalosis.

Apart from the factor of alkalosis, certain other pertinent references in the literature are worthy of our consideration here. Kochman and Kruger,[7] studying puerperal human uteri, found a decided change in the potassium-calcium ratio of this tissue over the ratio in the normal uteri, there being an increase in the potassium and a decrease in the calcium. Heller and Holtz,[8] in experiments with isolated guinea pig uteri, found that this shift greatly augmented the sensitivity of the uterus to pituitrin. Knaus and Clark,[9] likewise, have demonstrated that an increase in calcium caused a definite diminution in uterine tonus.

I mention the works of these investigators because of the importance they attach to the effects of these two elements on the sensitivity of the uterus and because there occurs a decidedly similar shift of these two elements during a period of maximum alkalosis. The decreased ionization of calcium in the swing to the alkaline side can be explained by the fact that calcium is insoluble in alkali and soluble in acid, and that it is mobilized from the bones in acidosis and returned to the bones by alkali.

A NEW METHOD FOR THE MEDICAL INDUCTION OF LABOR

With the idea of testing the thesis that the human gravid uterus is relatively more sensitive to pituitrin after complete alkalinization of the patient, 94 medical inductions were attempted on the alkalinized patient and the results compared with 113 inductions carried out according to the usual Mathieu[10] technique, and with 20 who were acidified, as controls.

These patients were selected at random from the Obstetric Clinic at Firmin Desloge Hospital with only one criterion prerequisite, i.e., the patient be at term.

All of these patients were either given 40 Gm. of sodium bicarbonate or 60 Gm. of Upjohn's "citrocarbonate," in divided doses, beginning the day before the attempted induction.

A study of the alkaline reserve was made before and after the ingestion of the bicarbonate by means of the carbon dioxide combining power determinations and urine pH changes. Blood pressure changes and side effects of the medication were also recorded. The intensity and number of uterine contractions were not measured by any definite standard, the only criterion for success or failure of the method being whether or not the patient went into labor after the injection of the pituitrin. After alkalinization, these patients were given a hot soap solution enema followed immediately by two-minim doses of pituitrin at twenty-minute intervals for a maximum of eight doses or until labor was established. Not infrequently only one or two doses of the pituitrin was necessary in order to initiate labor.

Side effects of the medication were practically nil. Most of the patients referred to a frequency of bowel movements but only two complained of vomiting the bicarbonate. In these cases, the dose was repeated at once. There was no evidence of fetal apnea or delayed respiration. Changes in the blood pressure were remarkably absent.

The carbon dioxide-combining power was raised an average of 14 volumes per cent by the alkali, and ranged in individual cases from a 6 to a 21 volumes per cent rise.

The urine pH varied from 6.5 to 9.0 after the bicarbonate and, in the majority of cases, was raised from 6.5 to 9.0.

Of the 94 inductions attempted, 65 succeeded, giving an efficiency of 70 per cent to the method.

In the control group, who were not alkalinized, there were 46 successes out of 113 attempts, or an efficiency of 44.6 per cent.

SERIES OF 20 PATIENTS MEDICALLY INDUCED AFTER ACIDIFICATION

Because of the establishment of the preceding facts, we can anticipate as a necessary corollary, that the gravid human uterus, after acidification, shall be relatively less responsive to pituitrin. Reasoning thus, we attempted twenty inductions after acidification with ammonium chloride.

The first 12 of this series received 4 Gm. of ammonium chloride daily for three days and were then subjected to an induction of labor identical to that in the alkaline series. Because we were unable to obtain a urine pH lower than 5.5 under this regime, the ammonium chloride dosage was increased to 6 Gm. daily on the remaining 8 patients.

The patients suffered no subjective symptoms referable to the acidosis.

The average figure for the alkaline reserve of these patients, after acidification, as studied by the carbon dioxide-combining power, was 46 volumes per cent. Compared with the average of 66 volumes per cent for the patients who were alkalinized, this shows a difference of 20 volumes per cent between the two series.

The urine pH averaged 5.5 for the 20 cases but ranged from 4.4 obtained in 5 cases to 7.2 obtained in 1 case. Of the 20 inductions only 3 succeeded, giving an efficiency rate of just 15 per cent to the method.

None of the attempted inductions was made before maturity. In fact, most of the cases were ideally suited for a successful induction, inasmuch as the fetal head was engaged in all cases and the average McDonald measurement was 36 cm. In no case was induction attempted with a McDonald below 34 cm.

TABLE I. SHOWING RESPONSE OF UTERUS TO PITUITRIN AFTER ALKALINIZATION, ACIDIFICATION AND MATHIEU TECHNIQUE OF INDUCTION

INDUCTIONS	NO. ATTEMPTED	NO. SUCCEEDING	PER CENT SUCCEEDING
After alkalinization	94	65	70.0
After acidification	20	3	15.0
According to Mathieu[10] technique	113	46	40.7

According to our experience with the original Mathieu technique, we have been unable to produce the high percentage of successful results claimed for it and have, therefore, sought a safe and more efficient method for the medical induction of labor. We firmly believe that the method of alkalinizing the patient before attempting the induction has produced, by far, the most satisfactory response of any heretofore published technique, excluding, of course, the various mechanical means with their attendant disadvantageous dangers.

It should be again emphasized that this series of inductions of labor, attempted after alkalinization, represents a group selected at random from the dispensary for the only reason that the patient had reached or passed her calculated term of gestation. The height of the uterus, engagement of the head, and thinning of the cervix were ignored. I feel that had we selected cases with deep engagement of the head and beginning effacement of the cervix our results would be even more impressive.

SUMMARY

Believing that there is a definite need for a more dependable technique of the medical induction of labor, and failing to achieve this end by utilizing the heretofore accepted routines, we have rather deviously hit upon a method, indirectly reached as a result of a previous study correlating the incidence of births with weather changes.

It is difficult to draw definite conclusions from a small series of 94 cases, but I believe that there lies here, at least, the nucleus of a theory suggesting the following:

1. The gravid human uterus, in vivo, responds more favorably to pituitrin after alkalinization.

2. Forty grams of sodium bicarbonate or 60 Gm. of "citrocarbonate," by mouth, in doses divided over a period of twenty-four hours, is an efficient alkalinizing agent.

3. Side effects of the medication are practically nil.

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4500 OLIVE STREET

TREATMENT OF POSTERIOR FACE PRESENTATIONS

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ALL reported studies of posterior face presentations have stressed the danger of this position to both mother and child. Reed[1] reported a maternal mortality of 11.6 per cent and a fetal mortality of 40.6 per cent. Recent statistics are lacking, but the predominant feeling is well summarized by De Lee[2] who concludes that "mentosacral positions terminating happily for the mother and child are so exceedingly rare that for practical purposes it is best to consider them as absolutely impossible and as always requiring interference from art." Taylor[3] and Penrose[4] as well as Reed long ago debated the absolute necessity for interference and quoted instances of spontaneous delivery of living infants. But they agreed that failure to rotate or advance was a definite indication for assistance.

Since Baudelocque[5] advocated manipulation in the treatment of face positions there has been much discussion regarding the necessity for such interference. Unanimity is not yet absolute but leading authorities agree that many anterior face presentations can be left to nature, intelligently supported. This policy has proved satisfactory on this service with the occasional assistance of low or midforceps.

The patients on whom this summary is based were treated on the maternity service of the Metropolitan Hospital, New York City, under the direction of Dr. H. E. Ayers. Treatment in each case followed individual consideration. Internal manipulations were performed under general anesthesia. The procedure used was dependent on the stage of labor at the time of discovery as follows:

A. Before the onset of labor (this occurred only once) the position was corrected successfully by the abdominal maneuver described by Schatz[6] in which the infant's chest is pushed strongly towards the occiput and up, while the breech is pulled in the opposite direction, automatically elevating and flexing the head. The diagnosis was corroborated by x-ray before and after correction. Occiput-anterior delivery occurred spontaneously two weeks later.

B. After the onset of labor: 1. With the cervix 2 fingers dilated, the combined internal and external maneuver described by Ziegenspeck[7] was used. Two fingers were inserted through the cervix disengaging the face and progressively flexing the head while an assistant used the "Schatz" maneuver to re-align the body. This was attempted once only in Case 6 and the position corrected but not maintained. A brow presentation without descent later resulted. Because of a borderline contracted pelvis in addition to good condition of mother and child, a trachelolaparotomy was resorted to with satisfactory results to both.

2. With the cervix three or more fingers dilated, the face was pushed up and the head flexed and guided into occipito-anterior position by the internal hand, while the external hand flexed the body and maintained fundal pressure as described by Thorn.[8] This was attempted in five cases and was successful in four. Spontaneous delivery followed in three, and the fourth was terminated by midforceps. All these infants survived and apparently were normal on discharge from the hospital.

3. With full dilatation of the cervix and a contracted uterus: The Thorn maneuver was attempted unsuccessfully in one such case (Case 3). This patient was then treated by manual rotation of the chin anteriorly and forceps delivery as a mentum anterior. Another patient (Case 2) was similarly treated by rotation anteriorly and forceps delivery, but without attempted conversion to occiput presentation. These were the two babies that did not survive the neonatal period, succumbing on the fifteenth day and after the sixth hour, respectively. Autopsies were obtained on both. The first confirmed the clinical impression of cerebral hemorrhage. The second occurred unexpectedly, and there were no definite internal abnormalities except cerebral edema.

4. The long neglected case in which the chin becomes impacted in the hollow of the sacrum, with the forehead still above the symphysis pubis is becoming less frequent. However, when it does occur the outlook is still very bad. Hebosteotomy,[9] craniotomy, and version are variously recommended, but all have serious objections and are certainly not ideal for all such cases. With this in mind, we believe the following case (Case 7) to be of unusual interest as it is to our knowledge the only report of a successful delivery from an impacted posterior face position by an extraperitoneal cesarean section. This choice of operation was guided by: (1) the long labor with ruptured membranes, (2) the tight uterus with a definite contraction ring, (3) small pelvis, and (4) the good condition of mother and child.

The operative technique followed was that recently developed and admirably described by Waters.[10] In addition to the logical simplicity of this extraperitoneal approach, the site of the low transverse uterine incision is ideal for the delivery of the hyperextended occiput, albeit some difficulty may be expected from the tightly contracted uterus.

Case History (No 10797).—(Case 7.) The patient was a young single primigravida of eighteen years admitted on March 17, 1940, three weeks before her estimated date of confinement. Pains had begun, however, three days before admission. Rupture of the membranes had occurred the day previously and for twelve hours there had been bearing down pains. The previous history was irrelevant and the ante-partum course had been normal. She had attended the antenatal clinic and no abnormalities had been noted on her last visit two weeks before admission.

The patient's general condition appeared good except for coryza and congested nares. Heart and lungs were normal. Pulse was 90 and blood pressure 122/90. The temperature was 99.4° F. The uterus seemed full term with the fundus 2 fingers below the xiphoid. Contractions were strong every three minutes. On the left suprapubically was a large cephalic prominence and just above was a persistent contraction ring. The fetal heart was regular, in the R.L.Q., with rate of 150. The uterus was tetanic. Over the vulva a bloody mucoid discharge was present. On rectal examination several irregular bony protuberances were felt with the mouth apparently posterior.

On vaginal examination the cervix was found fully dilated and retracted. The presenting part was the full face, edematous and bulging just below the spines. The chin was posterior and slightly to the right. No membranes could be felt. The chin was fixed and could not be dislodged upward or rotated anteriorly by firm pressure. The pelvic concavity was small with a deep sacral hollow. The promontory was hidden by the chin. The diagnosis was an impacted face presentation in the right mentum posterior position in second stage labor. X-rays confirmed the diagnosis and revealed a small inlet with an android posterior segment. External measurements were: interspinous, 20.0 cm.; intercristal, 23.5 cm.; external conjugate, 19.0 cm.; biischial, 8.0 cm.

Because of the long labor with ruptured membranes (more than sixty hours), lack of descent on bearing down, Bandl's contraction ring, small pelvis, fixation of face and good condition of mother and child, a supravesical extraperitoneal cesarean section was decided upon. The operation started at 2 P.M., March 17, 1940, and was conducted under spinal anesthesia, 120 mg. procaine and ½ c.c. of 1 per cent pantocaine. The operating time was sixty-five minutes.

Procedure.—A low left paramedian incision was made over a filled bladder and carried through skin, subcutaneous tissue, superficial and deep fascia, muscle separated easily, bleeding controlled with ligation. Transversalis and perivesical fascia were incised in midline down to bladder wall. Upper angle of this incision extended transversely across bladder below peritoneal reflexion. Perivesical fascia was elevated off bladder and pushed laterally by blunt dissection. Vesicouterine fold of fascia was identified in left upper angle and cut. Bladder was emptied, and this incision extended across fundus of bladder, thus cutting off vesicouterine fascial attachment to bladder and allowing latter to drop well down. Bleeding was controlled with ligation. Peritoneal fold retracted upwards. Uterine fascia incised transversely, and pushed up and down, thus exposing all of lower uterine segment. Contraction ring was identified. Upward curved transverse incision was made through uterine wall just below this contraction ring, vertex presenting in opening. Child delivered with vectis and fundal pressure. Ergotrate 1 c.c. given intravenously. Uterine wall was closed with two layers of continuous chromic gut No. 2. Peritoneal flap was pulled down intact over bladder. Penrose drain was inserted behind bladder in uterovesical space. Three heavy dermal tension sutures were placed. Fascia was closed with continuous chromic No. 2 catgut, interrupted around drain. Skin was closed with black silk interrupted vertical mattress sutures.

A normal male child, weighing 7 pounds, 5 ounces, was delivered and a normal respiratory rhythm was established after some difficulty. The hyperextension of the head gradually diminished during the first two weeks.

The blood pressure and pulse remained good throughout the operation, and there was very little postoperative reaction. The abdomen was always soft. Fluids were well taken and there was voiding spontaneously on the first postoperative day. Skin sutures were removed on the sixth day and tensions on the eleventh postoperative day. The patient was out of bed on the fourteenth and home on the seventeenth postoperative day. X-ray of pelvis post partum revealed an android type posterior pelvis with a converging fore pelvis. True conjugate diameter was 10.75 cm. (Thoms). Diameters of the fetal head at birth were: occipitofrontal 12.75 cm., and biparietal 10.0 cm. The patient was seen and examined the first and second months after discharge. Her general condition was good. The incision was well healed. The uterus was well involuted and in good position. There were no adnexal masses or bladder disturbances. The baby was healthy.

SUMMARY

The treatment of 8 cases of posterior face position in labor and of one before the onset of labor is described. The latter was converted to an occiput presentation by the abdominal maneuver of Schatz.

During labor four of these positions were converted by the Thorn maneuver to the occiput anterior and safely delivered. Two others were rotated to a mentum anterior and delivered as such with forceps. One patient was delivered by a low flap cesarean section, and one by a supravesical extraperitoneal cesarean section. There were no maternal deaths or stillbirths. The two infants delivered by forceps in the mentum anterior position died during the neonatal period apparently to the effects of birth trauma.

Version was not attempted in this series primarily because of (1) a contracted or borderline pelvis; (2) a tight, thin uterus with membranes long ruptured; and (3) an incompletely dilated cervix.

The etiology of this abnormal position was not always clear but one constant finding seemed to be relative disproportion between the size of the infant and pelvis. The pelvic asymmetry was demonstrated by the three small android pelves which we were able to check by x-ray, and the fetal factor by one large eleven-pound child and by one small five-pound, twelve-ounce child in a large multiparous woman. Multiparity and relaxed abdominal walls did not seem to be important, as there were four young primiparas with firm musculature and only two had had more than two children. A differential between primary and secondary dolichocephaly could not be established, but it is interesting to note that of the 6 babies whose head measurements were recorded, 5 had an occipitofrontal diameter of 12.5 cm. or greater. The exception was the small child mentioned above whose occipitofrontal measurement was 9.5 cm.

Early diagnosis and accurate determination of size and shape of pelvis are essential to the proper conduct of this type of dystocia. X-ray pelvimetry is of assistance but not always conclusive. Where definite cephalopelvic disproportion exists, cesarean section is the method of choice, except that in the cases where labor is far advanced the choice lies between extraperitoneal section, hebosteotomy, and craniotomy.

In the borderline case, conversion to the occiput anterior is the safest course. If descent does not then follow, forceps delivery must be added to the three procedures mentioned in advanced cases. In patients with ample pelves, spontaneous rotation to the mentum anterior is the rule. We believe that this explains the constant finding of small pelves in this group of persistent posterior face presentations. This also raises the question of the advisability of rotation to the mentum anterior and forceps delivery in cases with relatively contracted pelves. Extraperitoneal cesarean section and hebosteotomy are definitely less harmful to the infant.

CONCLUSIONS

1. Relative cephalopelvic disproportion is frequently found in posterior face presentations.

2. Manual conversion to the occipitoanterior position is feasible and is the safest form of delivery for both mother and child.

3. Version and extraction are contraindicated in many of these cases.

4. Forceps rotation to mentum anterior and delivery in this position resulted in high neonatal mortality.

5. Supravesical extraperitoneal cesarean section is a logical and practicable addition to the treatment of impacted posterior face presentations.

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THE TREATMENT OF GONORRHEAL SALPINGITIS WITH ESTROGENIC HORMONES

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GONORRHEAL infection of the adult female genital organs originates in the external genitalia. Skene ducts, Bartholin's glands, and the cervical glands are the sites of predilection of the infection. These depots of gonococci, especially in the cervical glands, constitute a steady menace to the Fallopian tubes. Invasion of the tubes takes place through a grass-like growth along the genital mucosa. An anatomic continuity of the mucosa for this purpose is indispensable.[1]

Observation on a large number of patients showed that the primary attack of gonorrheal salpingitis occurred at the time of menstruation, while only few and comparatively mild cases were observed in the postpartum and postabortal periods.

The biologic and physiologic functions of the Fallopian tubes are governed to a great extent by the follicular hormones. The follicular hormones increase the peristalsis and other movements of the tubes (Reynolds, S. R. M.,[2] Geist, S. M., Salmon, U. J., Mintz, M.[3]), animate the ciliary motion of the columnar cells, stimulate the proliferation of the tubal mucosa (Novak, E., Everett, H. H.,[4] Caffier, P.[5]), and promote the growth of the entire organ in case of infantilism (Clauberg, C.[6]). These effects in combination with others yet to be detected, add to the protective resistance of the tubes.

While one may attribute the relative scarcity of the gonorrheal-salpingitis attacks in the postgravid periods to the copious drainage and to the invasion of the uterine cavity by more potent germs; however, their mild character suggests an increased resistance of the Fallopian tubes to the gonorrheal infection at these times.

At the time of menstruation, the estrogenic hormone level drops and so the tubes are deprived of the beneficial action of the hormones, thus creating at menstruation a point of lowered resistance. Post-partum and postabortal, the drop in the estrogenic hormone level is not as drastic as at the time of the menstruation, and possibly the hormones of the involution substitute to some degree for the estrogenic hormones in the protection of the tubes against the gonococcic invasion. Therefore, it was believed that a maintenance of the follicular hormone level at the time of the menstruation might constitute a reasonable therapy in bridging over the "danger period." Furthermore, since proliferation and ensuing desquamation of the genital mucosa is the main weapon in the fight against a gonorrheal infection and since the estrogenic hormones stimulate this proliferation, an increase in the estrogenic hormone level in any phase of a gonorrheal salpingitis attack will be beneficial.

It was empirically estimated that 30,000 international units of follicular hormones, divided into three doses and given intramuscularly at the onset of menstruation would be sufficient for the bridging of the "danger period," while in the treatment of acute gonorrheal salpingitis, a daily injection of 10,000 international units was decided upon.

MATERIAL AND RESULTS

The above described treatment was instituted on Aug. 1, 1937. The patients were divided into two groups: Group I, patients with chronic salpingitis treated in the Out-patient Department of the Harlem Hospital; Group II, patients with acute salpingitis hospitalized on the wards.

Group I. Cases With Chronic Salpingitis.—To this group were admitted patients with one or more attacks of salpingitis, palpable adnexa or adnexal tumors, and abdominal discomfort. The conditions for admission were: normal temperature, sedimentation rate, and white cell count. These patients were treated with estrogenic hormones at the time of menstruation, and except for sedatives and vinegar douches, did not receive any other form of treatment.

Seventy-four patients were treated through 6 to 10 periods. Fourteen of these patients had been previously hospitalized for acute salpingitis. During the time of their treatment, there was no recurrence of salpingitis. Except for sporadic minor complaints, the patients steadily improved. Frequent gynecologic examinations disclosed a gradual decrease in the size of the adnexal tumors and in a large number of cases, complete disappearance. Two patients became pregnant.

A control group of 20 patients was treated for six months with distilled water injections instead of estrogenic hormones at the time of menstruation. Twelve patients showed a gradual improvement, 2 patients suffered an acute attack of salpingitis and 6 patients complained of stationary or increased discomfort and demanded a change in treatment.

Group II. Cases With Acute Salpingitis.—All these patients were hospitalized cases. They were divided into two groups:

Group A. Menstruating Group: To this group belonged patients who had their periods while hospitalized and were treated at this time with three injections of 10,000 international units of follicular hormones at three-day intervals. Fifty-four patients received such treatment. Seventy per cent of these cases had normal temperature during and after their periods, while 30 per cent continued to be febrile. In several instances, instead of the 10,000 international units, 3 times a week procedure, a daily injection of 4,000 international units was used and the results in these cases were slightly better than in the rest of the patients in the group. In a control group of 48 patients, who did not receive any treatment what-

soever, just the opposite results were obtained, i.e., 70 per cent of these patients continued to be febrile, and only 30 per cent had normal temperatures.

Group B: This group consisted of 37 patients whose attack of salpingitis did not follow a short term course and whose temperature remained constantly high despite the routine treatment. These patients were given injections of 10,000 international units of estrogenic hormones at daily intervals. While no percentual figures are claimed in these cases, the beneficial action of the injections was manifested by marked and occasionally dramatic improvement.

DISCUSSION

The only paper dealing with the treatment of gonorrheal salpingitis with follicular hormones was published in 1939 by Clauberg,[6] who obtained beneficial action from the use of the follicular hormones in cases of chronic gonorrheal salpingitis. He ascribes this effect to hyperemia, proliferation of the mucosa, and especially to growth of the entire tube. Several reproductions of salpingograms with re-established patency of the tubes were shown. 50,000 international units at five-day intervals between periods in conjunction with other types of treatment such as baths, diathermy, and short wave were employed. In his opinion, the growth of the whole organ, with a simultaneous enlargement of the tubal lumen was regarded as the most important factor in the re-establishment of the patency.

The treatment described in this paper was instituted two years previous to the publication by Clauberg and is based upon a somewhat different point of view. The dosages are much smaller.

Synthetic and biologic hormones of different types were used with equally good results. No discomfort or noteworthy disturbances in the menstrual cycle were observed.

The depots of gonococci in the external genitalia were not treated on account of the experimental status of these cases. It was regarded as essential to maintain the threatening foci intact to prove the value of the follicular hormone therapy in the prevention of re-infection of the tubes.

Naturally, in properly treated cases, the "bridged over periods" should be utilized for the cleaning up of these depots, to bring about a complete cure. A fairly large number of private patients treated in this manner with equally satisfactory results are not included in this paper.

CONCLUSION

A "danger period" exists at the time of menstruation when gonorrheal salpingitis attacks are likely to occur or re-occur. Thirty thousand international units of follicular hormones, divided into 3 doses and given intramuscularly at three-day intervals with the onset of menstruation are recommended for bridging over this "danger period." Injection of 10,000 international units of follicular hormones at frequent or daily intervals is suggested in the treatment of acute gonorrheal salpingitis.

Very satisfactory results were obtained with this treatment, in 74 cases of chronic salpingitis and 91 cases of acute salpingitis over a period of thirty months.

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ORAL PREGNENINOLONE IN THE TREATMENT OF SPONTANEOUS ABORTION

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THE purpose of this communication is to present the results of the treatment of a series of 50 consecutive cases of threatened and habitual abortion treated with oral pregneninolone.

All patients enrolled for obstetric care were given a supply of 5 mg. tablets of pranone* to have on hand. Those patients presenting a history of habitual abortion were instructed to take 10 mg. twice weekly until quickening occurred. In special cases, where a history of miscarriage in the later months of pregnancy was obtained, therapy was continued for a longer period. These patients were advised to record on a calendar the days that menstruation would occur if they were not pregnant. At this time their activity was restricted, and 10 mg. were given daily.

Patients with threatened abortion received a minimum of 10 mg. twice daily until all symptoms subsided, and then continued to take 10 mg. twice weekly for several months. Bed rest and occasionally barbiturates were the only other therapeutic measures. Morphine and its derivatives were not used because of the danger of stimulating uterine contractions.[1]

RESULTS (TABLES I AND II)

A total number of 50 patients were treated with oral pregneninolone. Of these, 39 were patients who threatened to abort during the present pregnancy and gave no history of previous spontaneous abortion. The remaining 11 patients gave a history of previous spontaneous abortion. There were a total of 8 failures. Seven of these failures occurred in the group of threatened abortions. Although 6 of the 11 habitual abortion patients threatened to lose the existing pregnancy, there was only one failure in this group. These results compare favorably with, and closely approximate, those obtained in similar groups of patients treated with progesterone.[1-3]

DISCUSSION

The value of the corpus luteum hormone, progesterone, in the treatment of spontaneous abortion has been demonstrated by numerous investigators. The experience of no less an authority on abortion than

*Pranone (anhydro-hydroxy-progesterone) supplied by the Schering Corporation.

Taussig[4] has been, as he describes, "most satisfactory." He further states that, "in view of the small number of therapeutic measures available, this one should be employed in every case of habitual abortion."

TABLE I

CASE	NAME	AGE	GRAV.	PARA	THREATENED	HABITUAL	DURATION OF GESTATION	RESULT
1	F. B.	28	iii	i	X	O	3 mo.	Normal baby at term
2	I. B.	27	iii	i	X	O	3 mo.	Normal baby at term
3	G. B.	30	i	0	X	O	4 mo.	Normal baby at term
4	H. C.	25	i	0	X	O	3 mo.	Failure
5	I. D.	20	iii	ii	X	O	6½ mo.	Normal baby at term
6	M. D.	32	ii	i	X	O	6½ mo.	Normal baby at term
7	R. D.	25	i	0	X	O	3 mo.	Normal baby at term
8	A. D.	22	iv	i	O	X	—	Normal baby at term
9	H. E.	26	i	0	X	O	3½ mo.	Normal baby at term
10	S. E.	22	i	0	X	O	2 mo.	Failure
11	J. F.	?	i	0	X	O	4 wk.	Failure
12	F. F.	26	i	0	X	O	2 mo.	Normal baby at term
13	H. F.	26	iii	0	O	X	—	Normal baby at term
14	M. F.	28	i	0	X	O	2 mo.	Normal baby at term
15	R. G.	24	i	0	X	O	4 wk.	Normal baby at term
16	S. G.	26	ii	0	O	X	—	Normal baby at term
17	S. G.	35	iii	0	O	X	—	Normal baby at term
18	B. H.	34	i	0	X	O	6 wk.	Normal baby at term
19	E. H.	20	i	0	X	O	2 mo.	Normal baby at term
20	H. H.	30	ii	i	X	O	2½ mo.	Failure
21	L. H.	29	iii	i	X	O	6 wk.	Normal baby at term
22	B. H.	24	iv	i	X	X	4 wk.	Normal baby at term
23	H. H.	35	iii	0	X	X	3 mo.	Failure
24	S. I.	34	ii	i	X	O	6½ mo.	Normal baby at term
25	J. K.	30	i	0	X	O	6 wk.	Normal baby at term
26	H. K.	24	i	0	X	O	3 mo.	Normal baby at term
27	S. M.	26	ii	0	O	X	—	Normal baby at term
28	A. R.	27	ii	0	X	X	3 mo.	Normal baby at term
29	H. R.	28	ii	i	X	O	3½ mo.	Normal baby at term
30	S. R.	32	i	0	X	O	2½ mo.	Normal baby at term
31	J. T.	32	ii	0	X	X	3 mo.	Normal baby at term
32	M. S.	25	iii	i	X	O	5 mo.	Normal baby at term
33	R. S.	25	i	0	X	O	3 mo.	Normal baby at term
34	B. S.	37	ii	i	X	O	3½ mo.	Normal baby at term
35	L. S.	25	ii	0	X	O	3½ mo.	Normal baby at term
36	W. W.	24	i	0	X	O	6 wk.	Normal baby at term
37	S. Z.	27	ii	i	X	O	6 wk.	Normal baby at term
38	T. F.	30	ii	0	X	X	6 wk. & 3 mo.	Normal baby at term
39	F. W.	32	ii	0	X	O	2½ mo.	Normal baby at term
40	H. S.	31	ii	0	X	O	6 wk.	Failure
41	R. F.	30	i	0	X	O	7 mo.	Normal baby at term
42	A. H.	33	i	0	X	O	2½ mo.	Normal baby at term
43	C. S.	20	i	0	X	O	6 wk.	Failure
44	R. L.	27	ii	0	X	O	6 wk.	Normal baby at term
45	R. E.	23	i	0	X	O	3 mo.	Failure
46	B. P.	31	i	0	X	O	6 wk.	Had myomectomy done at 4½ mo. Normal twins at term
47	J. W.	20	i	0	X	O	3 mo.	Normal baby at term
48	S. R.	21	i	0	X	O	3 mo.	Success. Undelivered as yet
49	G. F.	21	i	0	X	O	6 wk.	Success. Undelivered as yet
50	H. S.	28	iv	i	X	X	4 wk.	Success. Undelivered as yet

TABLE II

	NO. CASES	SUCCESS	FAILURE	PER CENT SUCCESS
Threatened abortion	39	32	7	82
Habitual abortion	11	10	1	91
6 of these patients threatened to abort during present pregnancy				
Total	50	42	8	84

The most recent and conclusive evidence in support of the logic of this form of therapy has been supplied by Browne, Henry, and Venning.[5] They demonstrated that patients with threatening and habitual abortion show low urinary pregnanediol excretions.

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We observed no undesirable or toxic effect in our series of cases with the preparation of oral pregneninolone which we used, although in many patients large doses were given over a period of many months. Our experience in treating gynecologic disorders also indicates that this material is innocuous.

CONCLUSIONS

1. A series of 50 patients with threatened and habitual abortion were treated with oral pregneninolone (anhydro-hydroxy-progesterone), and there were only eight failures.

2. The results obtained with oral pregneninolone compare favorably with and closely approximate those obtained using progesterone in oil.

3. Oral pregneninolone, although not as potent milligram for milligram as progesterone, presents numerous advantages.

4. No undesirable or toxic effects as the result of the administration of this drug were noted.

5. Oral pregneninolone is of distinct value in the treatment of threatened and habitual abortion.

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PRELIMINARY REPORT ON THE TRANSPORTATION OF MATERIALS FOR GONOCOCCAL CULTURES*

Lucile R. Hac, Ph.D., H. Close Hesseltine, M.D., Fred L. Adair, M.D., and Donald K. Hibbs, M.D., Chicago, Ill.

SOME months ago a study was undertaken for the purpose of evaluating certain measures of therapy in gonococcal infection in women. It was felt that cure must be based on negative cultures as well as smears. McLeod,[1] Carpenter,[2] Malcom[3] and others have amply demonstrated the value of cultures in the diagnosis of infection and have pointed out the probable advantages in determination of cure. Most of the results reported, however, have dealt with but one or two cultures from each patient. In determination of cure of infection, it is of considerable importance to know whether repeated consecutive smears may be negative while cultures remain positive.

*This work has been done under a grant from the Albert B. Kuppenheimer Foundation, Department of Obstetrics and Gynecology, The University of Chicago and The Chicago Lying-in Hospital.

Probably the majority of workers are convinced of the superiority of cultures over smears, but there are still many who feel that the methods are too difficult and impractical for routine use and that cultures can be reliable only if patients can be treated where laboratory facilities for immediate culture are available.

Because of these facts, it was believed that the data on smears and cultures accumulated in our study for the evaluation of therapies were worth reporting. In this study, the patients (all women) have been followed routinely by cultures and smears until they were discharged. A few of the patients were studied at the University of Chicago Lying-in Dispensary, but the great majority of them have been treated at the Chicago Municipal Social Hygiene Clinic* which is about five miles from the laboratory, thirty to forty-five minutes by trolley or elevated train which was the means of transportation used by most of the doctors who assisted in this problem. It was essential, therefore, to use some method of transportation of cultures and culture materials.

PROCEDURES

All necessary equipment, slides, swabs, broth tubes, and plates of media were transported from the laboratory to the Municipal Clinic in specially designed cases of ordinary suitcase size. The materials were left at room temperature until they were returned to the laboratory which was usually about five hours. No special precautions were taken to keep the materials warm during transportation even though the temperature on one occasion at least was -13° F.

In order that smear and culture material might be as comparable as possible, swabs were made with a minimum of cotton so that two could be inserted at the same time into the urethral or cervical canal. One swab was used directly to prepare the smear, the other was placed in a tube containing just sufficient nutrient broth to moisten the swab (0.2 to 0.3 c.c.). Better results were obtained when plates were inoculated with swabs so moistened than when they were used directly. The plates were inoculated as soon as possible, but when the clinic was crowded, it was sometimes two to three hours before materials could be plated. One-half plate was used for the cervical, the other half for the urethral cultures.

Practically all of the media reported in the literature in addition to certain experimental media have been tried in an effort to determine the best media and in the hope of devising a cheaper and simpler one. The results of that study will be reported elsewhere. All diagnostic cases were plated routinely on two media. Suffice it to say that the control media is still McLeod's chocolate agar. At first, media were poured three times a week, then twice, and now for some time they have been prepared but once a week. The method has been entirely satisfactory, provided the plates were stored in the refrigerator in well-covered cans.

The inoculated plates were returned to the laboratory and incubated at 35.5° C. in an atmosphere of about 10 per cent carbon dioxide. Incubator space was limited and so large airtight jars were impractical. One-pound coffee cans of approximate liter capacity which held four plates easily were used instead. The plates were put in the coffee cans and about 100 c.c. of carbon dioxide added from a small tank. The amount was determined by displacement of a measured volume of water. Plates were read at the end of 24, 48, and 72 hours. During the warm months of the year about 90 per cent of the cultures grew out in 24 hours, but during the colder months most strains required 48 hours. The number of strains which did not grow out until 72 hours was large enough to make incubation for the extra 24 hours necessary.

*These patients were made available through the Chicago Board of Health, Herman N. Bundesen, President, and Dr. G. G. Taylor, Director of Syphilis and Gonorrhea Section.

Usually colonies could be detected by direct inspection, but the oxydase test was used routinely for confirmation and as an aid in picking colonies from badly overgrown plates. Tetramethyl-p-phenylenediamine hydrochloride was used in preference to the dimethyl compound, because it did not kill the gonococcus, and with it, the gentian violet color appeared almost instantly as compared with one or two minutes when the dimethyl compound was used. Most workers seem to use the dimethyl compound in spite of its disadvantages because of the difference in price of the two compounds. Actually, the amount of material required is so small that price hardly needs to be considered. It is important that the solution be prepared fresh daily and, of course, if it were necessary to weigh out sufficient material to give an accurate 1 per cent solution, the expense might be great. A small amount of crystalline material about 0.5 cm. sq. heaped on the end of a spatula is sufficient for 10 c.c. of distilled water and that amount of solution is enough for 50 plates. The plates need not be sprayed with the reagent. One drop of solution is sufficient to confirm a suspicious colony, and three to four drops will moisten the surface of a heavily overgrown plate. For isolation it is better to pick colonies which have not been contaminated by the solution. An attempt was made to isolate as many strains as possible for future study. All strains isolated have been confirmed by fermentation tests.

NUMBER AND SOURCE OF SPECIMENS

Two hundred and sixteen patients have been considered in this study. It includes only patients in whom a diagnosis was made on the basis of isolation of the gonococcus and whose treatment was followed and cure determined by cultures. The [illegible] varied from 3 to 32; the minimum for any patient [illegible]

paper.

CONCLUSION

A "danger period" exists at the time of menstruation when gonorrheal salpingitis attacks are likely to occur or re-occur. Thirty thousand international units of follicular hormones, divided into 3 doses and given intramuscularly at three-day intervals with the onset of menstruation are recommended for bridging over this "danger period." Injection of 10,000 international units of follicular hormones at frequent or daily intervals is suggested in the treatment of acute gonorrheal salpingitis.

Very satisfactory results were obtained with this treatment, in 74 cases of chronic salpingitis and 91 cases of acute salpingitis over a period of thirty months.

TABLE I

DATE	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC			CHICAGO LYING-IN HOSPITAL				TREATMENT
				SMEAR		CULTURE		
				URETHRA	CERVIX			
	SMEAR	CULTURE	Hb	PUS CELLS	PUS CELLS	CERVIX	URETHRA	
12/ 5/39	-			- Many	- Epith.	4+	-	Local
12/12/39	-			- Many	- Many	-	-	
1/10/40	-			- Many	- Shreds	-	-	
1/25/40 Postmenstr.	-			- Mod.	- Epith.	-	-	
2/20/40	-			- Mod.	- Epith.	-	-	
2/28/40 Menses	-			- Many	- Few	-	-	
3/19/40	-			- Rare	- Mod.	4+	4+	
4/ 2/40	-			- Few	- Epith.	-	-	
4/15/40	-			- Few	- Epith.	-	-	

TABLE II

	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC	CHICAGO LYING-IN HOSPITAL		
		SMEAR	CULTURE	
		[illegible]	[illegible]	[illegible]

39 were patients who threatened to abort during the present pregnancy and gave no history of previous spontaneous abortion. The remaining 11 patients gave a history of previous spontaneous abortion. There were a total of 8 failures. Seven of these failures occurred in the group of threatened abortions. Although 6 of the 11 habitual abortion patients threatened to lose the existing pregnancy, there was only one failure in this group. These results compare favorably with, and closely approximate, those obtained in similar groups of patients treated with progesterone.[1-3]

DISCUSSION

The value of the corpus luteum hormone, progesterone, in the treatment of spontaneous abortion has been demonstrated by numerous investigators. The experience of no less an authority on abortion than

*Pranone (anhydro-hydroxy-progesterone) supplied by the Schering Corporation.

Taussig[4] has been, as he describes, "most satisfactory." He further states that, "in view of the small number of therapeutic measures available, this one should be employed in every case of habitual abortion."

TABLE I

CASE	NAME	AGE	GRAV.	PARA	THREATENED	HABITUAL	DURATION OF GESTATION	RESULT
1	F. B.	28	iii	i	X	O	3 mo.	Normal baby at term
2	I. B.	27	iii	i	X	O	3 mo.	Normal baby at term
3	G. B.	30	i	0	X	O	4 mo.	Normal baby at term
4	H. C.	25	i	0	X	O	3 mo.	Failure
5	I. D.	20	iii	ii	X	O	6½ mo.	Normal baby at term
6	M. D.	32	ii	i	X	O	6½ mo.	Normal baby at term
7	R. D.	25	i	0	X	O	3 mo.	Normal baby at term
8	A. D.	22	iv	i	O	X	—	Normal baby at term
9	H. E.	26	i	0	X	O	5½ mo.	Normal baby at term
10	S. E.	22	i	0	X	O	2 mo.	Failure
11	J. F.	?	i	0	X	O	4 wk.	Failure
12	F. F.	26	i	0	X	O	2 mo.	Normal baby at term
13	H. F.	26	iii	0	O	X	—	Normal baby at term
14	M. F.	28	i	0	X	O	2 mo.	Normal baby at term
15	R. G.	24	i	0	X	O	4 wk.	Normal baby at term
16	S. G.	26	ii	0	O	X	—	Normal baby at term
17	S. G.	35	iii	0	O	X	—	Normal baby at term
18	B. H.	34	i	0	X	O	6 wk.	Normal baby at term
19	E. H.	20	i	0	X	O	2 mo.	Normal baby at term
20	H. H.	30	ii	i	X	O	2½ mo.	Failure
21	L. H.	29	iii	i	X	O	6 wk.	Normal baby at term
22	B. H.	24	iv	i	X	X	4 wk.	Normal baby at term
23	H. H.	35	iii	0	X	X	3 mo.	Failure
24	S. I.	34	ii	i	X	O	6½ mo.	Normal baby at term
25	J. K.	30	i	0	X	O	6 wk.	Normal baby at term
26	H. K.	24	i	0	X	O	3 mo.	Normal baby at term
27	S. M.	26	ii	0	O	X	—	Normal baby at term
28	A. R.	27	ii	0	X	X	3 mo.	Normal baby at term
29	H. R.	28	ii	i	X	O	3½ mo.	Normal baby at term
30	S. R.	32	i	0	X	O	2½ mo.	Normal baby at term
31	J. T.	32	ii	0	X	X	3 mo.	Normal baby at term
32	M. S.	25	iii	i	X	O	5 mo.	Normal baby at term
33	R. S.	25	i	0	X	O	3 mo.	Normal baby at term
34	B. S.	37	ii	i	X	O	3½ mo.	Normal baby at term
35	L. S.	25	ii	0	X	O	3½ mo.	Normal baby at term
36	W. W.	24	i	0	X	O	6 wk.	Normal baby at term
37	S. Z.	27	ii	i	X	O	6 wk.	Normal baby at term
38	T. F.	30	ii	0	X	X	6 wk. & 3 mo.	Normal baby at term
39	F. W.	32	ii	0	X	O	2½ mo.	Normal baby at term
40	H. S.	31	ii	0	X	O	6 wk.	Failure
41	R. F.	30	i	0	X	O	7 mo.	Normal baby at term
42	A. H.	33	i	0	X	O	2½ mo.	Normal baby at term
43	C. S.	20	i	0	X	O	6 wk.	Failure
44	R. L.	27	ii	0	X	O	6 wk.	Normal baby at term
45	R. E.	23	i	0	X	O	3 mo.	Failure
46	B. P.	31	i	0	X	O	6 wk.	Had myomectomy done at 4½ mo. Normal twins at term
47	J. W.	20	i	0	X	O	3 mo.	Normal baby at term
48	S. R.	21	i	0	X	O	3 mo.	Success. Undelivered as yet
49	G. F.	21	i	0	X	O	6 wk.	Success. Undelivered as yet
50	H. S.	28	iv	i	X	X	4 wk.	Success. Undelivered as yet

TABLE II

	NO. CASES	SUCCESS	FAILURE	PER CENT SUCCESS
Threatened abortion	39	32	7	82
Habitual abortion	11	10	1	91
6 of these patients threatened to abort during present pregnancy				
Total	50	42	8	84

The most recent and conclusive evidence in support of the logic of this form of therapy has been supplied by Browne, Henry, and Venning.[5] They demonstrated that patients with threatening and habitual abortion show low urinary pregnanediol excretions.

The numerous advantages of oral therapy are easily recognized. It is a fact that there is a greater tendency for spontaneous abortion to occur at the expected menstrual time during the first few months of pregnancy. Physiologic investigations reveal that although, as a rule, ovulation ceases during pregnancy, the menstrual wave, as manifested by slightly increased body metabolism and increased nervous irritability, may persist for several months after conception in certain individuals.[4] It is at this time that corpus luteum hormone therapy should be emphasized because of its inhibitory action on uterine motility. It is important for those patients, giving a history of habitual abortion, to remain inactive and avoid traveling to the doctor's office for injection at this time. The convenience to the patient and doctor of having tablets available at home is noteworthy. All patients under the care of an obstetrician could be supplied with tablets of pregneninolone, so that in case any signs of threatened abortion appeared therapy could be started without delay. Patients who insist on taking long automobile, train, plane, or boat trips against the advice of their obstetrician can prophylactically take this material. The cost involved is considerably less than progesterone in oil and within the means of the average patient. In considering the dosage of oral pregneninolone to be used, the fact that it is approximately one-sixth as potent as progesterone must be taken into consideration. Furthermore, it is probable that progesterone in oil has a more immediate effect than orally administered pregneninolone. At the present time we are investigating the effect of oral pregneninolone on human uterine motility and urinary pregnanediol excretions. Hamblen[8] obtained no significant alterations in the urinary titers of sodium pregnanediol glucuronide and of androgens using this form of therapy. Cohen and Stein[7] believe that caution should be exercised when administering pregneninolone therapy in the human being. This attitude is based upon their animal toxicity experiments in which they demonstrated tubular necrosis in the kidneys and cloudy swelling and hyperemia in the livers of rats. They also report mild undesirable effects, such as nausea, vomiting, abdominal pain, weakness and dizziness, and headaches in 31 per cent of their clinically treated patients, although no serious reactions or evidence of liver or kidney injury was observed. This evidence of toxicity has not been confirmed by other investigators.

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1. A series of 50 patients with threatened and habitual abortion were treated with oral pregneninolone (anhydro-hydroxy-progesterone), and there were only eight failures.

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PROCEDURES

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Practically all of the media reported in the literature in addition to certain experimental media have been tried in an effort to determine the best media and in the hope of devising a cheaper and simpler one. The results of that study will be reported elsewhere. All diagnostic cases were plated routinely on two media. Suffice it to say that the control media is still McLeod's chocolate agar. At first, media were poured three times a week, then twice, and now for some time they have been prepared but once a week. The method has been entirely satisfactory, provided the plates were stored in the refrigerator in well-covered cans.

The inoculated plates were returned to the laboratory and incubated at 35.5° C. in an atmosphere of about 10 per cent carbon dioxide. Incubator space was limited and so large airtight jars were impractical. One-pound coffee cans of approximate liter capacity which held four plates easily were used instead. The plates were put in the coffee cans and about 100 c.c. of carbon dioxide added from a small tank. The amount was determined by displacement of a measured volume of water. Plates were read at the end of 24, 48, and 72 hours. During the warm months of the year about 90 per cent of the cultures grew out in 24 hours, but during the colder months most strains required 48 hours. The number of strains which did not grow out until 72 hours was large enough to make incubation for the extra 24 hours necessary.

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Usually colonies could be detected by direct inspection, but the oxydase test was used routinely for confirmation and as an aid in picking colonies from badly overgrown plates. Tetramethyl-p-phenylenediamine hydrochloride was used in preference to the dimethyl compound, because it did not kill the gonococcus, and with it, the gentian violet color appeared almost instantly as compared with one or two minutes when the dimethyl compound was used. Most workers seem to use the dimethyl compound in spite of its disadvantages because of the difference in price of the two compounds. Actually, the amount of material required is so small that price hardly needs to be considered. It is important that the solution be prepared fresh daily and, of course, if it were necessary to weigh out sufficient material to give an accurate 1 per cent solution, the expense might be great. A small amount of crystalline material about 0.5 cm. sq. heaped on the end of a spatula is sufficient for 10 c.c. of distilled water and that amount of solution is enough for 50 plates. The plates need not be sprayed with the reagent. One drop of solution is sufficient to confirm a suspicious colony, and three to four drops will moisten the surface of a heavily overgrown plate. For isolation it is better to pick colonies which have not been contaminated by the solution. An attempt was made to isolate as many strains as possible for future study. All strains isolated have been confirmed by fermentation tests.

NUMBER AND SOURCE OF SPECIMENS

Two hundred and sixteen patients have been considered in this study. It includes only patients in whom a diagnosis was made on the basis of isolation of the gonococcus and whose treatment was followed and cure determined by cultures. The number of cultures per patient varied from 3 to 32; the minimum for any patient discharged has been 17. One thousand six hundred and fifty-six cervical and 1,675 urethral smears and cultures have been compared. Only satisfactory smears and cultures have been included; i.e., if the culture was so badly overgrown as to be doubtful or if the smear was too thin or contaminated to be read (204 specimens), these reports have been deleted.

The reliability of initial diagnosis or of cure whether on the basis of smear or culture is largely dependent upon the technique used in the collection of material. Good smears are unquestionably more difficult to obtain in women than in men, but with care they can be prepared quite easily. It is important that the material be taken from sites which harbor the gonococcus, namely Skene's, Bartholin's, and endocervical glands. Material from the vagina or the vaginal introitus rarely contains gonococci after subsidence of the acute stage of the infection. Moreover, material from this area is usually so badly contaminated with vaginal bacteria that the slides are unreadable, and the cultures are overgrown.

The meatus of the urethra should be wiped dry with a piece of cotton to avoid inclusion of confusing vulvar bacteria. The finger should then be passed within the vagina, and the urethra firmly stripped from above downward against the pubic arch. A cotton swab or platinum needle may be used for collection of the material.

In order to obtain satisfactory specimens from the cervical glands, the cervix should be exposed with a speculum which has been inserted without lubrication other than water. The vaginal secretion should be wiped out and the plug of cervical mucus mechanically removed. The cervix should then be compressed with the speculum in order to force the secretion from the endocervical glands, and the material removed on a cotton swab inserted directly into the cervical canal. Some workers prefer to insert the swab and then compress the cervix.

RESULTS

The importance of cultures in the determination of cure can best be demonstrated by a few representative charts of patients on local treatment. Occasionally an erratic positive culture preceded and followed by negative cultures showed that the patient still harbored the organism although smears were never positive. These positive cultures frequently appeared during and just following the menstrual period.

TABLE I

DATE	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC: SMEAR	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC: CULTURE	Hb	CHICAGO LYING-IN HOSPITAL: SMEAR: URETHRA: PUS CELLS	CHICAGO LYING-IN HOSPITAL: SMEAR: CERVIX: PUS CELLS	CHICAGO LYING-IN HOSPITAL: CULTURE: CERVIX	CHICAGO LYING-IN HOSPITAL: CULTURE: URETHRA	TREATMENT
12/ 5/39	-			- Many	- Epith.	4+	-	Local
12/12/39	-			- Many	- Many	-	-	
1/10/40	-			- Many	- Shreds	-	-	
1/25/40	-			- Mod.	- Epith.	-	-	
Postmenstr.								
2/20/40	-			- Mod.	- Epith.	-	-	
2/28/40	-			- Many	- Few	-	-	
Menses								
3/19/40	-			- Rare	- Mod.	4+	4+	
4/ 2/40	-			- Few	- Epith.	-	-	
4/15/40	-			- Few	- Epith.	-	-	

TABLE II

DATE	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC: SMEAR	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC: CULTURE	Hb	CHICAGO LYING-IN HOSPITAL: SMEAR: CERVIX: PUS CELLS	CHICAGO LYING-IN HOSPITAL: SMEAR: URETHRA: PUS CELLS	CHICAGO LYING-IN HOSPITAL: CULTURE: CERVIX	CHICAGO LYING-IN HOSPITAL: CULTURE: URETHRA	TREATMENT
2/6/40	-			? Diplococcus	- Occasional	4+	4+	Local
2/15	-			- Occasional	- Shreds	4+	-	
2/20	-			- Few	- Shreds	-	-	
2/27	-			- Few	- Shreds	-	-	
Postmenstr.								
3/5	-			- Few	- Few	Overgrown		
3/18	-			- Epith.	- Shreds	-	-	
Menses								
3/29	-			- Epith.		-	-	
Postmenstr.								
4/5	-			- Mod.	- Epith.	+	+	
4/12	-			- Mod.	- Epith.	-	-	
4/19	-			- Many	- Shreds	-	-	

These patients might have been considered cured even in a clinic which required several consecutive negative smears for discharge. Table IV might explain some of the reported relapses in patients who had received chemotherapy but whose negative smears were not an indication of cure. Table V shows twelve patients whose cultures remained positive for more than two weeks after smears had become negative.

Notwithstanding the fact that cultures have been transported for several miles during all seasons and without special precautions for protection, they have proved to be far superior to smears as a criterion of cure. In women the status of infection is determined by smears and

Other patients showed persistent positive cultures although the smears were consistently negative.

cultures from both cervix and urethra. Since one or both sites may be involved, Table VI presents the results of both cervical and urethral smears as compared with cultures.

The smears have been examined very carefully. Even after long search there are many slides in which typical diplococci can be found extracellularly but not intracellularly. These slides have been further subdivided into those in which the diplococci were found in typical clump formation and those in which only scattered unclumped organisms were found.

TABLE III

DATE	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC		Hb	CHICAGO LYING-IN HOSPITAL						TREATMENT AND PROGRESS NOTES
				SMEAR				CULTURE		
				CERVIX		URETHRA				
	SMEAR	CULTURE		PUS CELLS		PUS CELLS		CERVIX	URETHRA	DRUG AND DOSAGE	
10/23/39	+										Routine examination. No symptoms
10/30/39	+		65%	+	Many	-	Mod.	4+	4+	Local	Asymptomatic
11/13/39	-			-	Many	-	Few	4+	4+		Asymptomatic
11/16/39				-	Occ.	-	Epith.	4+	4+		Feels well
11/20/39	-			E†	Many	-	Epith.	4+	4+		Asymptomatic
11/27/39	-			-	L. bac	-	Mod.	4+	og*		
12/ 4/39	-			E‡	Many	-	Few	4+	-		Feels well
12/ 7/39	-			-	Few	-	Many	2+	-		Profuse mucoid cervical discharge
12/11/39				-	Mod.	-	Few	3+	-		Discharge. Denies contact
12/14/39	-										
12/18/39	-			-	Few	-	Epith.	-	-		Discharge decreased
12/26/39	-										
1/ 8/40	-			-	Many	-	Epith.	2+	-		No complaints. Discharge decreasing
1/15/40	-			-	Many	-	Epith.	-	-		Asymptomatic
1/22/40	-			-	L. bac	-	Epith.	2+	-		Profuse vaginal discharge
2/ 5/40	-			-	Mod.	-	Epith.	4+	-		Denies contact. Moderate discharge
2/ 7/40											
3/ 4/40	-			-	Mod.	-	Epith.	-	og*		Discharge. Denies contact
3/11/40	-			E	Mod.	E	Epith.	og*	og*		Asymptomatic. Moderate discharge
3/18/40	-			-	Many	-	Epith.	4+	4+		Urethra slightly inflamed. Cervical discharge
4/ 1/40	-			-	Few	-	Epith.	-	-		Profuse discharge
4/15/40	-			-	Mod.	-	Epith.	4+	4+		Purulent discharge. Denies contact

*Overgrowth.
†Typical extracellular diplococci in clumps.
‡Lactobacillus.

Of the positive cultures, only 27.7 per cent had corresponding positive slides; 19.8 per cent had clumps of typical extracellular diplococci; 8.0 per cent had scattered typical extracellular diplococci; and 44.5 per cent had completely negative smears. Only four smears with intracellular organisms and nine smears with typical extracellular organisms had corresponding negative cultures (0.56 per cent), in spite of the fact that there was frequently a delay of two or three hours in the inoculation of plates and an interval of four to five hours before incubation.

When cervical and urethral smears and cultures are compared separately, the results are even more striking (Table VII). Urethral smears are considerably less reliable than cervical smears as an indication of

TABLE IV

DATE	CHICAGO MUNICIPAL SOCIAL HYGIENE CLINIC		CHICAGO LYING-IN HOSPITAL								TREATMENT AND PROGRESS NOTES
					SMEAR			CULTURE			
					CERVIX	URETHRA					
	SMEAR	CULTURE	Hb	Bl. LEVEL	PUS CELLS	PUS CELLS		CERVIX	URETHRA	DRUG AND DOSAGE SULFANILAMIDE	
1/30/40	+		70%		E Few	- Shreds		3+	3+	4 Gm. p. 4	Vaginal discharge, endocervicitis
2/ 2/40					- Few	- Epith.		2+	2+		
2/ 6/40	-		75%	4.6 mg.	- Few	- Epith.		+	-	3 Gm. q. 4	Moderate cervical discharge
Post-menstr.											
2/13/40	-				- Occ.	- Few		+	+		Missed drug one day. Urethra clean. Cervix inflamed
2/16/40					- Mod.	- Few		og.*	og.*	Discont.	Slight discharge
2/23/40					- Epith.	- Epith.		-	-		Slight discharge

*Og. = overgrown.

TABLE V. POSITIVE CULTURES AFTER SMEARS HAD BECOME NEGATIVE

PATIENT'S NUMBER	NO. OF DAYS	SITE
311	126	Urethra and cervix → Cervix
314	50	Cervix
316	23	Urethra and cervix
320	19	Urethra and cervix → Cervix
321	25	Cervix
328	86	Urethra and cervix
359	49	Urethra and cervix
375	36	Urethra and cervix
396	33	Urethra and cervix
423	51	Urethra and cervix
426	33	Urethra and cervix
452	30	Urethra and cervix

TABLE VI. COMPARISON OF SMEARS AND CULTURES OF CERVIX AND URETHRA COMBINED

		NO.	% OF + CULT.	% OF TOTAL
Patients cultured		216		
Total cultures		1598		
Total + cultures		535		33.5
Smear	Culture			
+	+	148	27.7	9.3
E*	+	106	19.8	6.6
?†	+	43	8.0	2.7
-	+	238	44.5	14.9
+	-	4		0.25
E*	-	9		0.56
?†	-	19		1.19
-	-	1031		64.5

*Typical extracellular diplococci in clumps.
†Typical extracellular diplococci, but no clumps

TABLE VII. COMPARISON OF SMEARS AND CULTURES

		CERVIX			URETHRA		
		NO.	% OF + CULT.	% OF TOTAL	NO.	% OF + CULT.	% OF TOTAL
Patients cultured		216			216		
Total cultures		1,656			1,675		
Total + cultures		548		33.1	405		24.2
Smear	Culture						
+	+	129	23.5	7.8	33	8.1	2.0
E*	+	93	17.0	5.6	50	12.3	2.7
?†	+	42	7.7	2.5	42	10.4	2.5
-	+	284	51.8	17.1	280	69.1	16.7
+	-	5		0.3	1		0.05
E*	-	10		0.6	3		0.2
?†	-	19		1.2	6		0.4
-	-	1,074		64.8	1,260		75.2

*Typical extracellular diplococci in clumps.
†Typical extracellular diplococci, but no clumps.

infection. Only 8.1 per cent of the positive urethral cultures were associated with positive smears, 69.1 per cent with completely negative smears. Twenty-three and one-half per cent of the positive cervical cultures were associated with positive smears; 51.8 per cent with negative smears.

In this connection it is important to know whether both sites of infection respond to treatment equally well. Table VIII gives the incidence

TABLE VIII. INCIDENCE OF VARIATION OF CERVICAL AND URETHRAL CULTURES

	NO. OF PATIENTS	NO. OF TIMES	TIMES PER PATIENT	NO. OF DAYS
Cervix +, urethra -	32	73	2-11	7-51
Cervix -, urethra +	10	14	2- 5	7-40

of variation of cervical and urethral cultures. Forty-two patients showed one site positive and the other negative for more than two consecutive times. Usually the cervix is the most resistant site of infection, but occasionally the residual infection is found in the urethra. Smears are even less reliable here.

SUMMARY

1. Cultures have been used routinely to determine the cure of gonococcal infection in women in various types of therapy.

2. Cultures have been found to be reliable and far superior to smears even when (a) Culture materials were not plated for two or three hours after they had been taken; (b) Plates were not incubated for four to five hours after they had been inoculated; (c) Plates were transported from the clinic to the laboratory (thirty to forty-five minutes) in all kinds of weather without special precautionary measures.

3. Cervical smears were more reliable than urethral smears, but even with them, over 50 per cent of the positive cultures had corresponding negative smears.

4. In the majority of cases both cervical and urethral sites of infection cleared simultaneously. In residual infections the cervix was more frequently the resistant site.

5. Tetramethyl p-phenylendiamine hydrochloride is preferable to the dimethyl compound for the oxydase test.

Acknowledgment.—The authors wish to express their appreciation for the cooperation of Drs. S. Charles Kasdon, Jack Kight, Robert G. Greene, and Lewis L. Hall of the Chicago Lying-in Hospital, who assisted in the collection of culture materials and in the examination of slides.

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CLINICAL EXPERIENCE IN THE TREATMENT OF PELVIC INFLAMMATORY DISEASE WITH INTRADERMAL INJECTIONS OF BACILLUS COLI VACCINE

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THIS paper presents the clinical result obtained in the ambulatory treatment of pelvic inflammatory disease of venereal and puerperal etiology following the intradermal administrations of a suspension of *B. coli.* The intradermal method of administration was found to be easier to execute, less uncomfortable and more safe than either the intramuscular administration of "boiled milk" or the intravenous administration of typhoid vaccine. Yates and Davidow reported over 3,000 intramuscular injections of boiled milk without the occurrence of an abscess, but I have encountered four such instances, two of which patients were hospitalized for over two months. Obviously, intravenous shock therapy cannot be used in ambulatory patients.

This report represents the first group of 172 cases in our investigation, which began in July, 1933. There was no selection of patients and no other medical treatment was administered except placebos for the control of severe pain and douches for cleanliness.

PREPARATION OF THE VACCINE

The first vaccine used was a suspension of *Staphylococcus aureus*, which was discarded because of the relatively large amounts required to produce a reaction. The colon bacillus was then selected, and a vaccine containing one-half billion organisms per cubic centimeter was used. This concentration was gradually increased until our present vaccine, in use during the last four years, contains three billion organisms per cubic centimeter.

Mrs. Edith Hamilton, chief bacteriologist, prepared these vaccines in the laboratories of Receiving Hospital. A culture was obtained from a fresh stool specimen, grown on agar and put up in normal saline containing 0.5 of 1 per cent of trieresol. This material was used when negative cultures were obtained on three successive days and in the absence of spores. Specimens of this material standing at room temperature were found sufficiently potent at the end of sixteen and thirty months, respectively.

Our one experience in sterilizing with heat resulted in the destruction of the active agent and our clinical results approached zero.

It is an interesting observation that the most commonly used vaccines for the production of foreign protein shock therapy contain the bacillary form of organisms, i.e., typhoid, colon, lactic acid.

METHOD OF ADMINISTRATION

The technique of administration was the same as that employed in the "Schick test," followed by gentle massage. A needle of 22 or 24 gauge was of distinct advantage.

The injections were made at least six inches apart to avoid the necrosis that follows Arthus' phenomenon. The thigh was the site of preference because small areas of local induration and discoloration may be present for as long as six weeks.

An arbitrary number of six injections was selected to constitute "a series" or course of treatment. The injections were given twice weekly if the reactions were not too severe, otherwise, once weekly. Two weeks after a series was completed a re-examination was done, and a decision was made as to whether additional treatment or a change of treatment was advisable.

The initial injection was one-fourth cubic centimeter. Each successive dose was increased by one-fourth cubic centimeter up to a maximum of one cubic centimeter.

Occasionally when the local reaction was too severe or too small the initial amounts were varied so that a local reaction of several days' duration was obtained which was followed by a local area of induration at the site of the needle puncture.

EFFECTS OF ADMINISTRATION

The effects of the administration of the *B. coli* suspension have been similar to those obtained after the administration of other forms of so-called shock therapy, except that in the majority of cases they have been less severe.

The local effect was swelling, redness, pain, and temperature. A few days after the administration of the vaccine a small area of induration appeared at the site of injection and would frequently remain for several weeks. Occasionally subsequent injections brought about a reoccurrence of initial symptoms at the site of previous administrations. In a few

cases small areas of necrosis occurred when successive injections were injudiciously placed too close together.

The effect upon the pelvic pathology was also similar to other forms of shock therapy. Exaggeration of the pelvic symptoms might occur followed by improvement of the pain. In the majority of cases the pelvic pain was relieved to a great extent following three or four injections. The vaginal discharge also lessened. An interesting situation occurred in a number of cases which puzzled us in the beginning of our investigation. Following a series of treatments and the two weeks' waiting period, the women would come in for the check-up examination complaining bitterly there had been no relief of their pain and presumably of their illness. Abdominal and vaginal examinations revealed a practically normal pelvis. The uterus was freely movable without pain; there were no adnexal masses or areas of induration of the broad ligaments; there was little or no vaginal discharge. We have attempted to explain this situation by suggesting that the original inflammatory process had not subsided about, or in, the sensory nerves as rapidly as it had subsided in the other tissues. Additional therapy was found to be not necessary. In private practice these cases have been helped by heat induced by the high frequency current.

The general effects of the vaccine were similar to those experienced in other forms of shock therapy. Malaise, dizziness, headache, nausea, vomiting, diarrhea, chills, fever, etc., might appear in any combination and intensity in from three to twelve hours. These reactions would last for several hours to a day or two. The changes in temperature and pulse rate taken at two-hourly intervals following intradermal administrations were followed in fifty instances. The average temperature rise was 1.8° F., which lasted on an average of 4.1 hours. Coincidently, the average rise in pulse rate was 17.9 beats per minute.

CLINICAL STATISTICS

In this series the white patients numbered 76, the blacks, 96.

Eighty-eight patients had been hospitalized from two to seven days prior to discharge to the outpatient department for medical therapy.

The follow-up periods averaged 11.4 months following the last treatment.

TABLE I. SERIES OF VACCINE GIVEN AND MONTHS OF TREATMENT GIVEN

NUMBER OF SERIES OF SIX INJECTIONS	CASES	NUMBER OF MONTHS OF TREATMENT	CASES
Less than one	8	Less than one	3
One	122	One	118
Two	35	Two	27
Three	5	Three	10
Four	1	Four	3
Five	1	Five	2
		Six	3
		Seven	3
		Nine	1
		Fifteen	1
		Forty-two	1
Total	172	Total	172

The first part of Table I shows the number of series of injections given to these cases. Almost 96 per cent received two series or less. The second part of Table I shows the number of months of treatment that each case required. With added experience fewer patients were treated longer than three months. The case requiring forty-two months (five series) was cured by removal of the cervical focus. Eighty-six per cent of these patients responded in two months or less.

Table II presents the cases of patients (13.3 per cent) under treatment for three months or longer. The patients who had colpotomies were treated after operation except for one who developed an abscess during the first series of injections.

Part one of Table III presents the complications found in those patients who required two or more series of vaccine. In part two, showing the number of cases requiring three or more series, attention is drawn to the outstanding number of patients with residual cervical infection.

TABLE II. PATIENTS REQUIRING TREATMENT FOR THREE MONTHS OR LONGER

Required treatment	9
Chronic cervicitis	5
Colpotomy done	5
Uterine retroversion	2
Pyosalpinx	3
Total	24

TABLE III. COMPLICATIONS FOUND IN PATIENTS REQUIRING TWO OR MORE SERIES OF VACCINE

REASONS FOR TWO OR MORE SERIES	CASES	REASONS FOR THREE OR MORE SERIES	CASES
Irregular treatment	3	Irregular treatment	
Chronic cervicitis	11	Chronic cervicitis	5
Colpotomy	5	Colpotomy	
Required treatment	18	Required treatment	1
Abdominal operation advised	3	Abdominal operation advised	
Pyelitis	1	Pyelitis	
Uterine retroversion	1	Uterine retroversion	1
Total	42	Total	7

TABLE IV. CASES REQUIRING OPERATION

Colpotomy	12
Bartholin abscess	3
Conization of cervix	12
Cautery of cervix	12
Abdominal section	7
Abdominal section refused	3
Total	49

Table IV presents those patients whose condition required both surgical and medical care (28.4 per cent). The complication most frequently encountered was a residual cervical infection, comprising 48.9 per cent of all surgical complications. Abdominal section was advised in 5.8 per cent. Interestingly, three of this group refused operation because they were relatively free of symptoms but still carried a mass that was diagnosed as pyosalpinx.

RÉSUMÉ

The intradermal administration of foreign protein in the treatment of pelvic inflammatory diseases is practical, more safe, and less uncomfortable for the patient.

The results obtained in the present series are briefly:

1. Eighty-six per cent required treatment, two months or less.

2. Ninety-six per cent required two series of six injections or less.

3. Twenty-eight and four-tenths per cent of these patients required some surgical procedure during the treatment of their illness. Only 5.8 per cent were advised to have radical abdominal surgery; only 4 per cent consented to abdominal section.

NOTE: I wish to express my appreciation for the untiring effort and cooperation of the resident and attending staff without which this work would not be possible.

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1551 WOODWARD AVENUE

ANTUITRIN-S SKIN TEST FOR EARLY PREGNANCY

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THE necessity for a rapid, inexpensive, and reliable test for pregnancy has stimulated for the past ten or more years a great deal of clinical and laboratory research. Unfortunately most of the optimistic claims for one method or another have been disproved by collaborative work on these tests. The various techniques have been numerous, each having a definite group of supporting investigators and varied periods of popularity. The Visscher-Bowman chemical test of the urine and the Gruskin-Schwartz antigen skin test are but two of these. Certain men have placed much confidence on the observation of the vascular tree.

More recently a considerable amount of work has been done, using antuitrin-S skin test as a means of rapid diagnosis of early pregnancy. Gilfillen and Gregg and others stimulated new interest in this test because of their very promising claims, in spite of the fact that others had tried the same test with very discouraging results. In its favor are the simplicity of its administration and the rapidity of diagnosis; on the surface the test seems well-founded physiologically.

The test is based upon the fact that associated with early pregnancy and continuing for many months, there is found a tremendous rise of the anterior pituitary-like hormone. It has been reported that the hormone excreted will rise from 150 units to over 100,000 units in the first month or two of pregnancy; there is a complete drop by five days post partum. It would seem natural, therefore, that in a pregnant patient saturated with this hormone, the introduction of a small quantity of this same substance intradermally should elicit no reaction. On the other hand, the same quantity introduced in a nonpregnant patient should stimulate a positive reaction.

All of the details of technique as specified in previous publications were rigidly adhered to in our series. Fresh solution was always employed, and when not used was kept in an ice box. Two minims were injected with an intradermal needle in the skin of the ventral surface of the forearm and the resulting wheal was observed for at least half an hour. A positive reaction was indicated by an area of erythema varying in diameter from 7 to 40 mm. around the site of the original injection; this signified an absence of pregnancy. A negative reaction was taken to signify pregnancy. In addition, 2 minims of normal saline solution was injected into the opposite forearm for control purposes.

This series is composed of 523 cases. Preparatory to this series 50 patients of known pregnancy were tested at random just to acquaint the authors with the possible variations of the reaction. It was during this period that the first discouraging factor was encountered, namely, the great number of atypical reactions. Ordinarily pregnant patients should show no erythema, but three definite types were found:

a. The immediate temporary reaction: In this group a few patients developed an immediate erythema which disappeared in five to ten minutes.

b. Delayed temporary reaction: In this group several patients developed an erythema after twenty minutes or more which lasted for about ten minutes.

c. Delayed prolonged reaction: In this group there were several patients in whom, after about six hours, an intense erythema developed which persisted for about twenty-four hours.

These reactions were not like those described as a positive reaction over 7 mm. which developed generally in a few minutes and persisted for a period of half an hour or more, indicating an absence of pregnancy.

The second discouraging factor was found when 100 nurses, through the cooperation of the Superintendent, were tested as controls. Of this group, 12 developed no reaction, signifying a positive test for pregnancy. There were, of course, no nurses pregnant in this group, and a 12 per cent error was obvious, therefore. Furthermore, 50 female patients of the medical convalescent ward, definitely not pregnant, were skin tested with the following results: 5 developed no reaction, signifying a positive test of pregnancy. Likewise, 50 patients from the male convalescent ward were skin tested with the result that 8 developed no reaction, signifying a positive test. The large discrepancy in this control series was very disappointing.

From the prenatal clinic 300 patients were picked at random for skin testing, irrespective of age or duration of pregnancy. Of this group of known pregnant patients, 21 developed a definite positive reaction signifying an absence of pregnancy. The discrepancy in this group was 7 per cent. Two patients in whom ectopic pregnancy was suspected were skin tested and showed a positive reaction which contradicted the diagnosis. Both of these patients were operated upon and, as the tests had indicated, there was no pregnancy.

Because so many patients in a municipal hospital are colored and this test would not be applicable, an effort was made to develop the conjunctival test. This was done by instilling two drops of antuitrin-S

into the conjunctiva at the same time the forearm test was performed. Unfortunately, after several hundred tests this procedure was abandoned because the eye shows an extremely poor response even when the forearm showed reactions as large as 20 mm.

TABLE I. PATIENTS AND CONTROLS SKIN TESTED WITH ANTUITRIN-S

DIAGNOSIS	NUMBER OF CASES	NEGATIVE REACTION	POSITIVE REACTION	PERCENTAGE OF ACCURACY
Definitely Pregnant	300	279	21	93
Nonpregnant				
a. Nurses	100	12	82	88
b. Convalescent female patients	50	5	45	90
c. Convalescent male patients	50	8	42	84
d. Post partum: 5 days—2 weeks	11	8	3	28
e. Abortions (complete)	10	6	4	40
f. Suspected ectopic pregnancy (ruled out by operation)	2	0	2	100

TABLE II. COMPARATIVE ANALYSIS OF RESULTS

AUTHORS	PREGNANT		NONPREGNANT	
	% CORRECT	% INCORRECT	% CORRECT	% INCORRECT
Porges-Pollatschek	71	29	95.4	4.6
Gilfillen-Gregg	100	--	100.0	--
Hoffman-Fough	71	29	80.0	20.0
Parsons	66	34		
Frank-Wahrsinger	68	32		
Mandy-Mandy	93	7	72.0	28.0

The average duration of pregnancy, which gave a positive pregnancy test, was four months; the shortest was in one patient who reported to be five days overdue in her period. Many positive tests of pregnancy were found in patients only one month pregnant by history. All questionable cases where any doubt existed were either checked by careful follow-up or by doing a Friedman's test.

In reviewing Table I, it is interesting to note that the incidence of correct results was much higher in the pregnant group than in the nonpregnant group. It is also interesting to note that so high a percentage of patients from five days to two weeks post partum persisted in showing positive tests for pregnancy even when laboratory data have shown that the hormone excreted practically disappears after five days post partum.

In reviewing Table II, it should be mentioned that Frank and Wahrsinger used a variety of preparations but did get a 68 per cent accuracy with the antuitrin-S. However, from the entire series, 98 per cent gave a positive (nonpregnant) skin reaction. Dr. Susanne Parsons, in her work, has felt that all hormonal preparations, regardless of the variety or by whom used, have proved universally unreliable.

SUMMARY AND CONCLUSIONS

1. So far as the authors can ascertain, this is to date the largest case series in which this test has been employed.

2. Rigid adherence to detail, critical analysis, and interpretation of results were attempted in the hope of ending the controversy upon this subject.

3. All questionable cases were carefully followed up or had a Friedman's test performed.

4. The conjunctival test was not adaptable as an adjunctive procedure.

5. The test requires a moderate amount of experience in order to acquaint the clinician with the typical and atypical reactions.

6. The reactions apparently do not vary with the age of the patient.

7. A positive test (negative reaction) only lends weight to a suspected diagnosis of pregnancy.

8. Its value is limited in colored patients.

9. This test is not an adequate substitute for the Friedman's or Aschheim-Zondek test.

10. Results: Of the pregnant patients, 93 per cent were diagnosed correctly and 7 per cent incorrectly. Of the nonpregnant patients, 72 per cent were diagnosed correctly and 28 per cent incorrectly.

Our appreciation is expressed to the Superintendent of Nurses, Gallinger Hospital, Washington, D. C., for the cooperation of the 100 nurses used in the control series; to Dr. Paul Dickens, George Washington University Medical School, Department of Medicine, for his generous supply of antuitrin-S; and to Dr. Howard F. Kane, Professor of Obstetrics and Gynecology, George Washington University Medical School, for his kind cooperation in the preparation of this paper.

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Mönckeberg in considering the etiology of vaginismus emphasizes that spasm which is palpably due to an organic lesion may often have had a psychic initiation. Each case must be investigated with patience and understanding. The author recommends the use of a cocaine ointment in selected cases in which it is felt that a demonstration that intercourse can actually be effected will give the needed reassurance to the patient.

Gradual dilatation with bougies should accompany psychotherapy when indicated. Having the patient bear down and contract the abdominal muscles strongly facilitates the introduction of the dilator as the vaginal sphincter and transverse perineal muscles relax at that moment. In some cases of dyspareunia, Mönckeberg makes a vertical incision through the posterior fourchette and underlying muscles, partly within the vagina and partly through the perineum. The incision is closed transversely, increasing the size of the introitus. Coitus is allowed after one month.

R. J. Weissman.

THE FETAL MOTION FACTOR IN THE ROENTGENOGRAPHIC DIAGNOSIS OF PREGNANCY*

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THE purpose of this paper is twofold: First, to demonstrate the possibility of error in roentgenographic diagnosis of pregnancy due to movement of the fetus, and second, to give a few suggestions in technique, possibly to eliminate this error.

The roentgen ray has proved very helpful to the medical profession in the diagnosis of pregnancy. There are, however, certain weaknesses in this valuable method of diagnosis. It was noticed recently in one of my patients that a twin pregnancy showed evidence of only one baby in the radiographic study. Further studies then brought out the shadow of the two babies.

A search was made through the literature. It became evident that the roentgenologists have been aware of the value of lack of fetal motion in the production of good pictures of the baby in utero. It also became evident that the clinicians have not realized the possibility of the complete lack of demonstration of fetal structures in the roentgenogram due to movement of the baby. Several cases have been reported in clinical magazines, where a fetus failed to be shown on the film. Other causes, however, than fetal motion were attributed as the etiology for the lack of roentgenographic demonstration.

Grier[1] advised that both lateral and anteroposterior views should be taken in the roentgen study for pregnancy. He was of the opinion that in early and in multiple pregnancy, the lateral view is more reliable than the anteroposterior view. He stated that in the later months of pregnancy, however, after the fetal head has dropped into the mother's pelvis, the fetal head is not well seen in the lateral view because of being obscured by the pelvic bones. The head then shows better in the anteroposterior view, and the trunk and extremities in the lateral view. He gave several reasons which he thought made the roentgenographic diagnosis of twin pregnancy difficult. He stated that the mother's abdomen is always larger and often the amount of amniotic fluid is considerable. He thought that, if the pregnancy is early, these factors might prevent the demonstration of fetal bones in the anteroposterior view but that they would be seen in the lateral view, due to the rays not having to go through so much tissue. He further stated that in late twin pregnancy with one fetus a head presentation and the other a breech, the two fetal heads would be at opposite ends of the abdominal cavity and a 14 by 17 plate might be too small to show both heads. Then often the other bones might be too faintly outlined to demonstrate two babies.

Anderson[2] reported two cases of twin pregnancy where anteroposterior roentgenographic exposures showed only one fetus in each film. One of his cases was a vertex-breech presentation. He thought it likely that the 14 by 17 film was not large enough to show the fetal pole in the uterine fundus. He stated that in a case like his second, in which both fetuses were cephalic, that one of the heads must be posterior to the other and therefore only one skull might show in the anteroposterior view.

In 1939, McGaha,[3] Chief Technician, X-ray Department, Touro Infirmary, New Orleans, Louisiana, advised as to the possibility of the radiograph's not giving

*Presented at a meeting of the Northern Minnesota Medical Association, at St. Mary's Hospital, Duluth, Minn., July 20, 1940.

evidence of fetal bones, due to movement of the baby. He showed radiographs of a monstrosity. The fetus could not be demonstrated in the first anteroposterior film but was present in the lateral and second anteroposterior views. He explained the lack of demonstration in the first study as due to a state of continuous motion of the fetal structure which did not allow a shadow to be cast.

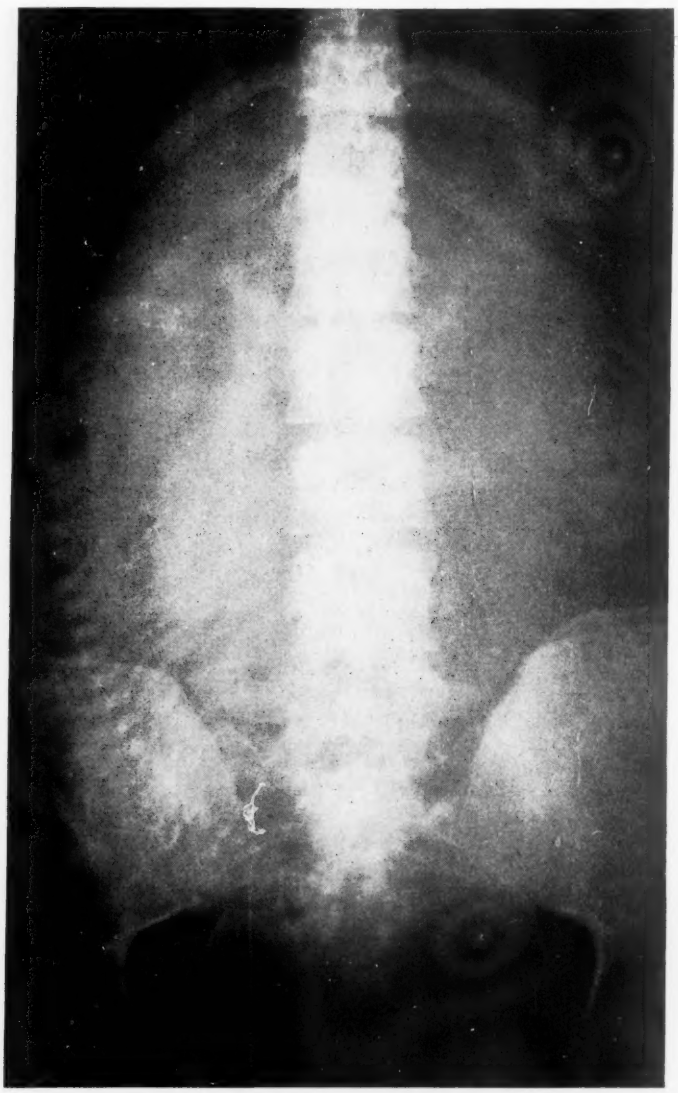

Fig. 1.—First anteroposterior roentgenogram of the mother's abdomen, revealing a single pregnancy.

This is the only reference in any journal, as far as I could ascertain, of the complete obliteration, due to fetal movement, of all fetal structures in the radiograph. This report was published in *Radiography* by the Eastman Kodak Company. The author of the article is a technician and not a physician.

The editor of *Radiography* suggested that the x-ray technician should forego the actual exposure until the fetus had stopped moving. He stated that a cooperative patient could tell when this had taken place.

CASE REPORT

Mrs. E. L., a 22-year-old white primipara, was admitted to St. Luke's Hospital on April 15, 1940, for roentgenographic study of the abdomen. The first day of her last menstrual period was Aug. 10, 1939. Considerable movement had been felt since the latter part of December, 1939. The date of expectancy was May 17, 1940.

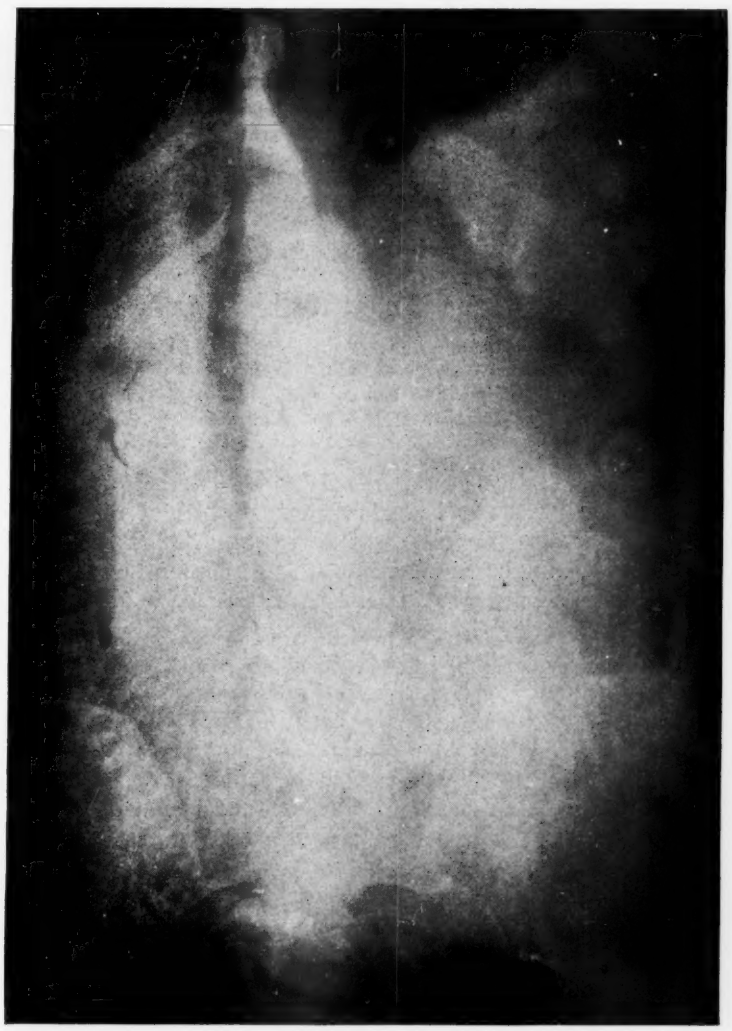

Fig. 2.—Second anteroposterior roentgenogram of the mother's abdomen, revealing a multiple pregnancy.

The prenatal period was uneventful, with the exception that as pregnancy progressed the patient's abdomen was larger than the usual size for a given gestational period. At the time of the eighth-month prenatal visit, April 15, 1940, it was thought that there might be two fetal hearts present, one in the lower left and

the other in the lower right quadrant. There was, however, only a difference of five heartbeats between the two areas, the counts being 140 and 145, respectively. An area that felt like a fetal back was present in each anterior and lateral portion of the mother's abdomen. Consequently the roentgenographic study was done as previously stated on April 15, 1940.

Anteroposterior and lateral roentgenograms of the mother's abdomen were taken. The anteroposterior view showed one fetus, with the head in the pelvis, in occiput right position. The appearance of the bones seemed to indicate an eight months' pregnancy. A lateral view was then taken. Two fetuses were distinctly present, both heads were down, one head was in the pelvis and the backs were slightly posterior. An anteroposterior film was immediately retaken. This time there were distinctly two fetuses. Both heads were down. The right head was in the pelvis. The backs were on the right and left sides of the mother's abdomen. Both babies had the appearance of about an eight months' pregnancy. When the roentgenographic study was completed, the mother stated that there had been considerable fetal movement during the taking of the first anteroposterior picture. The films were taken each immediately following the preceding one; the same technique was used each time; two anteroposterior and two lateral views were taken; both fetal heads presented in the pelvis and the mother herself stated that there had been much movement during the first study. It is, therefore, thought by me that the movements of one of the babies was the sole cause of lack of fetal demonstration in the first study. I feel further that such factors as hydramnios, the rays having to go through too much maternal tissue, the film being too small as might occur with a breech-head twin presentation, omitting the lateral views and so not having a complete study, played no part in my case.

The patient had a spontaneous delivery of two identical male twins on April 29, 1940. They were born after approximately six hours of labor. The first baby weighed 2,335 Gm., and the position was occiput right posterior to occiput right anterior. The second twin weighed 2,680 Gm., and the position was occiput left posterior to occiput left anterior. The mother had an uneventful puerperium and the babies progressed nicely.

As I stated earlier, there have been a few cases of false roentgenographic diagnoses of pregnancy previously reported in the literature. Two cases were given by a physician. The reasons he attributed for the lack of x-ray findings were other than fetal motion. The other case was reported by a technician, not a physician. He felt that continuous fetal motion was the cause of his not being able to demonstrate the baby on his first film.

This motion factor has actually been utilized in certain fields in roentgenology. According to Jacobs,[4] Ottonello,[5] in 1930, described a method of producing roentgenograms of the entire cervical spine in posterior projection on a single film. This method consisted of the roentgenogram taken with the jaw in constant vertical motion. Several complete motions of the jaw must be made, open and shut, during the exposure. By this method the mandible is "fanned" out and does not cast a shadow on the film. It is thereby possible to show the cervical vertebra from the second down on one film.

Elward and Belair[6] advised taking at least three roentgenographs so as to obviate the possibility of nonvisualization of fetal parts from movement. They also advised that a cleansing enema be taken several hours before the examination. They suggest that sufficient time be taken so that the patient does not become unduly excited. They think it a good plan to run an exposure or two first. This will show the patient the length of time necessary for her to hold her breath.

Hubeny and Delano[7] believed that the lateral roentgenogram has not received sufficient emphasis for its value in the diagnosis of pregnancy. They advise the abdominal binder for compression of the abdomen and immobilization of the fetus.

They instruct the patient to take a breath and hold it several seconds before making the exposure. They feel that this helps to quiet fetal movement.

DISCUSSION AND SUMMARY

From a search through the literature, it is evident that the roentgenologists have been and are aware of the value of lack of fetal motion in the production of good pictures of the baby in utero. It is, however, also evident that the clinicians do not realize the value of this moving fetus factor. As far as I could ascertain, no cases of complete obliteration of fetal structures have been reported by clinicians in the literature.

It is suggested that, in order to eliminate if possible this diagnostic error, the lower bowel and bladder should be empty at the time of examination, both anteroposterior and lateral roentgenograms should be taken, and the exposure not made until both the mother and fetus are quiet.

I am indebted to Dr. Gage Clement of the X-ray Department, St. Luke's Hospital, and Dr. Arden L. Abraham of the X-ray Department of St. Mary's Hospital, Duluth, Minn., for their help in the interpretation of the radiographs.

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PRIMARY EPIDERMOID CARCINOMA OF THE VULVA COMPLICATING PREGNANCY

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PRIMARY squamous cell carcinoma of the vagina and vulva is reputed to be a disease of the aged. When found complicating pregnancy in the young, it is indeed rare. Five cases of carcinoma of the external genitalia associated with pregnancy have been reported in the literature.

Review of the Literature.—The first case of squamous cell carcinoma of the vagina complicating pregnancy appeared in the French literature in 1929, reported by Audebert and Estienny.[1] This patient was a 33-year-old white multipara who had had slight genital bleeding and a serosanguineous discharge since the fifth month of pregnancy. She was in labor six hours, membranes had been ruptured artificially, but the head failed to engage. Consultation revealed a large tumor mass that had infiltrated the entire posterior vaginal wall. The child was delivered successfully by cesarean section. Biopsy was reported positive for squamous cell carcinoma of the vagina. The mother at the time this case was reported was alive and attending the cancer center for radium therapy. There was no complete follow-up in this case.

Tuft[2] in 1930 reported a case of carcinoma of the vagina associated with pregnancy in a 16-year-old negress. She was first seen when she was about seven and one-half months pregnant. Vaginal examination at that time revealed a cauliflower-like mass involving the upper two-thirds of the posterior vaginal wall, extending to the cul-de-sac but not involving the cervix or anterior vaginal wall. Biopsy showed squamous cell carcinoma of the vagina. The patient received preoperative radiation by means of radium needles implanted in the mass. Several days later cesarean

section was done; a living child was delivered which died shortly after birth. Patient's course was progressively downhill and death occurred six weeks after operation. Permission for autopsy was refused.

The following year, Baldwin[3] recorded a case of primary carcinoma of the vagina in a 14-year-old white girl. She was two and one-half months pregnant when the diagnosis was made. In spite of inadequate radium therapy she continued on to term and was delivered by classical cesarean section; this case due to extensive pelvic infiltration was considered inoperable and was treated with x-ray alone. She became rapidly worse and died fifteen months after delivery.

Mengert,[4] in 1935, reported a case of primary carcinoma of the vagina in a 21-year-old white primipara. This patient was admitted close to term with a history of a bloody, vaginal discharge which had occurred intermittently during the last trimester of pregnancy. On vaginal examination a slightly irregular, firm mass 2 to 3 cm. in diameter was palpated in the upper left fornix of the vagina. On direct vision the mucosa over the mass was slightly reddened, but otherwise normal. It was thought to be a cervical fibroid which would not complicate vaginal delivery, since it would rise with the formation of a lower uterine segment. After thirty-six hours of labor the cervix was only 10 cm. dilated and the tumor mass was larger than before. Delivery was effected by craniotomy and embryotomy. The patient was discharged on her nineteenth post-partum day, the nature of the mass still unknown, to return in two months for excision of the growth. She returned later with urinary retention and increasingly severe constipation and was, in general, very ill. Vaginal examination was difficult for the vagina barely admitted one finger; the entire vagina and pelvis were infiltrated. Biopsy revealed primary epidermoid carcinoma of the vagina. She died several days later from uremia. Autopsy revealed generalized involvement of the pelvis, vagina, and peritoneal cavity.

Russell,[5] in a recent report, recorded a case which closely parallels our own. He reported a case of primary squamous cell carcinoma of the vulva in a 19-year-old negress who at the time of diagnosis was in the seventh month of pregnancy. After radical vulvectomy she was delivered at term by cesarean section. The patient was further treated by radium and deep x-ray therapy and at the present time (after five years) shows no evidence of local recurrence or distant metastasis.

Age Incidence.—According to previous writers, malignancy of the vulva and vagina rarely occurs before late middle or old age. Williams[6] states that primary carcinoma of the vagina generally occurs between the ages of 50 and 60 years. In Rothschild's tabulation of 331 cases of vulval carcinoma, the incidence was greatest in the 60- to 70-year group. Hoffman,[7] reporting a series of 20 cases, found only 3 below the age of 50, and all were in the fourth decade. Taussig, quoted by Ludwick,[8] stated the average age for carcinoma of the vulva to be 59 years, and in another report the same author found that 60 per cent of the patients were over 60 and 30 per cent over 70 years of age. Baldwin, who has reported the youngest case accompanying a co-existing pregnancy, gives in the same communication the age distribution of 28 uncomplicated cases of vulval carcinoma. The greatest incidence occurred between 65 and 70. There were none under 30 years. In our case and in the five cases collected from the literature the ages vary from 14 to 33 years.

CASE REPORT

M. U., Case No. 117172, a 26-year-old, white female, gravida iii, para 0, was first seen in the Dermatologic Outpatient Dispensary on March 25, 1939. She complained of a large fungating mass of the right labia which had been present for the past seven months. It had started as a small, hard mass about the size of a marble and had steadily increased in size. Three months before admission it had ulcerated. At the same time she had noticed several pea-sized warty nodules on the left labia majora which had not grown during the last seven months. There was no history of syphilis or of inguinal lymphadenopathy. Her last menstrual period had been on Sept. 8, 1938. She had noticed marked breast changes and progressive increase in the size of her abdomen. She had not received any prenatal care nor had she consulted a doctor about the labial lesion until March 21, 1939, when she presented herself at the Health Center Prenatal Clinic for examination.

She was then referred to the Cincinnati General Hospital where she was seen by the Dermatological, Obstetrical, Gynecological and Tumor Clinic Departments. A provisional diagnosis of carcinoma of the vulva associated with six and one-half months' pregnancy was made, and the patient was sent into the hospital for treatment.

Past History.—The patient had had the usual childhood diseases, and had had typhoid fever at the age of 16. She was treated for pellagra two years prior to the present admission.

Catamenia began at the age of 14 years, occurring every twenty-eight days and lasting for four days. Patient had no previous gynecologic disorders or operations. She had had two previous pregnancies, both terminating in spontaneous abortions at the third month.

Physical Examination.—Temperature was 98.6° F.; pulse, 80; respiration 20; and blood pressure, 125/75. Patient was a well-developed, well-nourished, young white female, and did not appear acutely ill or in distress. Examination of the heart and chest was essentially negative. Abdomen was negative except for an intrauterine pregnancy, extending 2 to 3 fingers above the umbilicus. Vertex was presenting and not engaged, back on left, small parts on right, fetal heart 142 and regular.

Fig. 1.

Fig. 2.

Vaginal Examination.—On the right labium majus a large ulcerated fungating mass, measuring 6 cm. in diameter, was found (Fig. 1). The base of the tumor had infiltrated the labia, but the mass was movable and not fixed to the deeper structure. It partially obstructed the vaginal introitus, but did not involve the vaginal mucous membrane. Scattered over the upper part of the right labium majus and over the entire left labium majus there were numerous papillary and pedunculated nodules which were firm, nontender, and varied in size from 2 to 8 mm. They appeared like typical condylomata acuminata. Internal examination revealed a soft, nondilated cervix which pointed down and forward. The uterus was enlarged to about six and one-half months' gestation. Speculum examination revealed no infiltration or abnormalities of the vaginal mucous membrane or cervix.

Rectal examination was essentially negative. Small, soft inguinal glands were palpated bilaterally.

Blood Wassermann and vaginal smears were negative. Frei tests were read as strongly positive on the left arm and negative on the right arm. A biopsy was

taken on March 25, 1939, and was reported as epidermoid carcinoma, Grade III malignancy. X-ray examination of the pelvis and long bones showed no evidence of metastasis. After consultation between the Obstetrical, Gynecological, and Tumor Service, the following plan of treatment was decided upon:

1. Simple vulvectomy immediately to remove the local tumor mass and not to disturb the co-existing pregnancy.

2. Cesarean section when pregnancy had progressed sufficiently to insure a living child.

3. Bilateral radical groin dissections (Basset operation) as soon after delivery as patient's condition would permit.

4. Deep and superficial x-ray therapy to groin and vulva as soon as surgical wounds were healed. Radiation would also affect castration.

March 31, 1939, following our plan, a simple vulvectomy was done under general anesthesia by Dr. J. Heiman of the Gynecological Service. The patient was discharged with good results on May 8, 1939, to Prenatal Clinic. (Fig. 2.) No evidence of local recurrence was found.

On June 13, 1939, the patient, then in her eighth month of pregnancy, was admitted to the hospital for cesarean section. A classical section was done so as to avoid dissemination of tumor cells. A 6-pound 3-ounce male infant was delivered in good condition. The postoperative course was afebrile and the mother and baby were discharged on June 26, 1939.

The patient was readmitted on Oct. 4, 1939, for radical groin dissection. The lapse of time between the cesarean section and the groin dissection was much longer than originally planned because the patient refused to come in for operation. However, on Oct. 6, 1939, under gas-ether anesthesia, the femoral and inguinal glands on the left side were radically excised. Because of the length of this procedure only one side was done at that time. The right groin was dissected on Oct. 16, 1939. The pathologic report on the tissue removed showed no evidence of malignancy and the diagnosis of chronic lymphadenitis was made.

The period of convalescence was complicated by the filling of the dead space in the right groin with a serosanguineous sterile fluid which required repeated aspiration. On Nov. 14, 1939, the patient was discharged and referred back to the Tumor Clinic.

X-ray therapy was begun on Nov. 30, 1939, and completed Dec. 14, 1939. A total of 1400 r. units was given through 15 by 15 cm. ports to each groin, and a total of 1200 r. units was given directly to the perineum through a 10 by 10 cm. port. The factors were 200 K.V.; 15 MA; T.S.D.—50 cm.; 1 mm. Thoreus filter.

The patient was again hospitalized on Dec. 18, 1939, for incision and drainage of a subcutaneous abscess which had developed in the region of the right groin dissection. She also had a low-grade thrombophlebitis and cellulitis of the right leg and foot. After drainage of the abscess and conservative therapy to the leg, she convalesced rapidly and was discharged on Jan. 19, 1940. At the present time (after seventeen months), the wound in the groin is completely healed and the patient is in excellent health. No evidence of local recurrence or distant metastasis of the carcinoma can be found.

SUMMARY

Six cases of primary epidermoid carcinoma of the external genitalia complicating pregnancy, including the present report, have been recorded in the literature. Four had their primary site of origin in the vagina. Three of these ended fatally in a remarkably short time, the fourth patient was alive six weeks post partum. The final course is not known since the follow-up is incomplete. Two cases were primary squamous cell carcinoma of the vulva and were treated in a similar, though quite independent, manner. Both patients at the present writing are alive and well, one after a period of five years, the other after seventeen months.

The treatment of all operable carcinomas of the vulva is vulvectomy with complete bilateral inguinal dissection. This procedure must be tempered to fit the individual case when accompanied by pregnancy. The results of surgery for this condition are highly favorable. Taussig[9] reported 20.4 per cent and Stoeckel[10] a 31.2 per cent five-year cure rate. However, it is important to remember that these cases were not complicated by co-existing pregnancy.

According to Cutler[11] the effect of radiation therapy alone is difficult to evaluate. Variations in the character of the disease and the small number of cases studied constitute the chief difficulties. The difficulties surrounding radiation treatment of carcinoma of the vulva are due chiefly to the fact that the normal tissues of this region are so delicate and so sensitive to irradiation that it is exceedingly difficult to effect the sterilization of the carcinoma without serious damage to the normal tissues.

In the treatment of carcinoma of the vagina complicating pregnancy, surgery is not practicable. The therapy, therefore, is irradiation alone. Early diagnosis followed by the same thorough irradiation as is given for cervical carcinoma is important. The prognosis at best is poor.

CONCLUSION

1. A case of primary epidermoid carcinoma of the labia majora complicating a six and one-half months' pregnancy in a woman of 26 years is presented.

2. Treatment was instituted according to the following plan: Simple excision of the tumor mass, cesarean section, bilateral radical groin dissection, postoperative x-ray therapy.

3. Five other cases of carcinoma of the external genitalia complicating pregnancy in young women were collected from the literature. We agree with Russell that more cases must have occurred but were not reported.

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PRIMARY PNEUMOCOCCIC PELVIC PERITONITIS IN AN ADULT; PROMPT CURE BY SULFAPYRIDINE THERAPY

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PRIMARY peritonitis due to the pneumococcus in an adult is not frequent; when it is confined to the pelvis, it is rare indeed. In 1938 Nuckols and Hertig[1] were able to collect from the literature but 77 cases; only 23 of these were not associated with a recent obstetric episode. In 1940, Bennett and Mengert[2] added 2 cases. In 1939, Barnett, Hartmann, Perley and Ruhoff[3] reported the use of "sulfapyridine" in the treatment of pneumococcic peritonitis in 5 children, all of whom recovered. In 1939, Ladd, Botsford and Curnen[4] recommended the use of "sulfapyridine" in pneumococcic peritonitis in infants and children. A search of the literature has not revealed a report of the use of "sulfapyridine" in primary pneumococcic peritonitis, pelvic or general, in an adult.

CASE REPORT

On April 15, 1940, Mrs. E. N., a graduate nurse, aged 41 years, widow for two years, presented herself at the office. Four days previously she had first noted a profuse, irritating, greenish vaginal discharge which was accompanied by a mild diarrhea and occasional cramps in the lower abdomen. Two days later pain appeared in both lower quadrants of the abdomen, and diarrhea and cramps became worse. The same day for the first time, she had a temperature of 101° F. and

nausea, but no vomiting occurred. She had been on duty for over fourteen months with an aged male patient with a draining empyema cavity from which pneumococci and tubercle bacilli were said to have been recovered elsewhere. Except for an appendectomy about twenty years ago she had been well all her life; had never been pregnant and menstrual history had been unremarkable until four months previously, when a mild menometrorrhagia appeared and has continued. Last menstrual period was fourteen days before present illness. Coitus for the past two years was denied. There had been no cough or other respiratory difficulty. Examination revealed: Temperature, 100.4° F.; pulse, 96; respirations, 20; nose and throat clear and without discharge; lungs without evidence of pathology; abdomen, an old right rectus incisional scar, tenderness 1-plus in both lower quadrants, no spasticity or rebound pain; pelvis, a profuse, greenish yellow, blood-streaked discharge from the cervix, pain 4-plus upon motion of the cervix, especially upon lifting it forward, pain 3-plus to 4-plus throughout the pelvis, with generalized thickening but no masses, palpation difficult and unsatisfactory due to extreme pain. Smear made from the cervical discharge (Gram stain) showed many pus cells, polymorphonuclears; many red blood cells; many gram-positive extra-

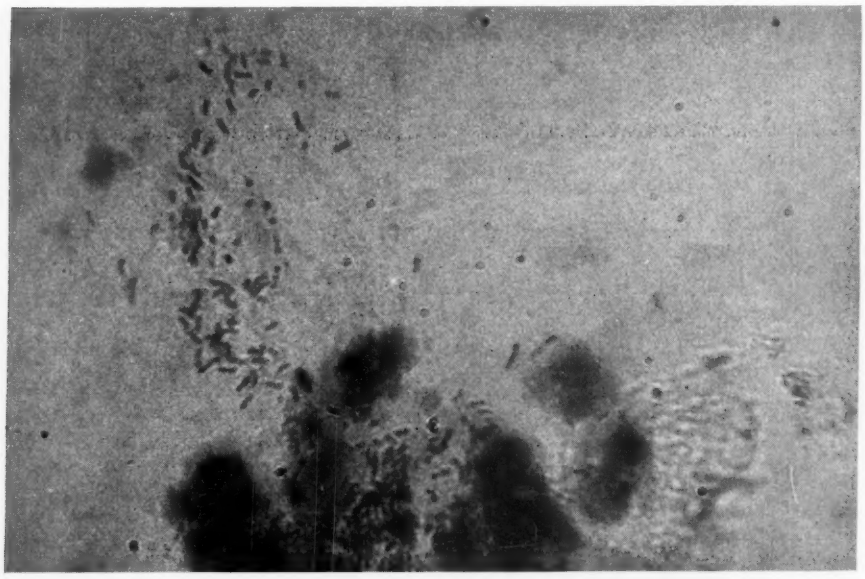

Fig. 1.—Photomicrograph of cervical smear, showing gram-positive extracellular encapsulated diplococci.

cellular encapsulated diplococci resembling pneumococci; no intracellular organisms. Material for typing and culture was obtained from the cervix upon sterile swabs and later taken to the hospital where it was reported they had dried to such extent that typing was impossible; culture was made, nevertheless, but showed no growth. Complete blood count showed hemoglobin 60 per cent; red blood cells 3,280,000; white blood cells 12,950; Schilling differential, neutrophiles 79 per cent, segmenteds 49 per cent, band forms 29 per cent, juvenile forms 1 per cent, lymphocytes 21 per cent. Early primary pneumococcic pelvic peritonitis was diagnosed, and she was admitted to St. Francis Hospital, admission No. 19233, at 6 P.M., April 15, 1940, where chest films showed no pathology. Sulfapyridine therapy was begun at once: 2 Gm. at each of the first 2 doses, four hours apart; then 1 Gm. every four hours, awakened if necessary; soda bicarbonate 4 Gm. with each of the first 3 doses of "sulfapyridine," then 3 times a day; fluids only as desired for the first eighteen hours, then to be forced to 3000 c.c. per twenty-four hours. pH of the urine was done at each voiding and remained at 7.5 throughout, otherwise normal. Nausea

was experienced the following day, April 16, and that evening she was given intravenously 500 c.c. of one-sixth molar sodium lactate solution and 500 c.c. of citrated blood. The next day, April 17, "sulfapyridine" concentration in the blood was 6.65 and that afternoon the dosage was reduced to 1.5 Gm. every eight hours for 3 doses, when it was discontinued. Total amount of "sulfapyridine" given: 16.5 Gm. in 13 doses, from April 15, 7 P.M. to April 18, 8 A.M. Only liquids, but including gelatin mixture, were allowed through April 19. Because of the secondary anemia, 1 c.c. of "reticulogen," was given each day of April 17, 18, 19. Temperature fell to normal on April 16 and, except for a slight rise on April 18, remained down; pulse and respiration came to normal on April 16 and remained so.

On April 18 complete blood count showed hemoglobin 78 per cent; red blood cells 4,020,000; white blood cells 5,000; Schilling differential, neutrophiles 71 per cent, segmenteds 58 per cent, band forms 12 per cent, juvenile forms 1 per cent, eosinophiles 3 per cent, lymphocytes 26 per cent. Blood culture taken on April

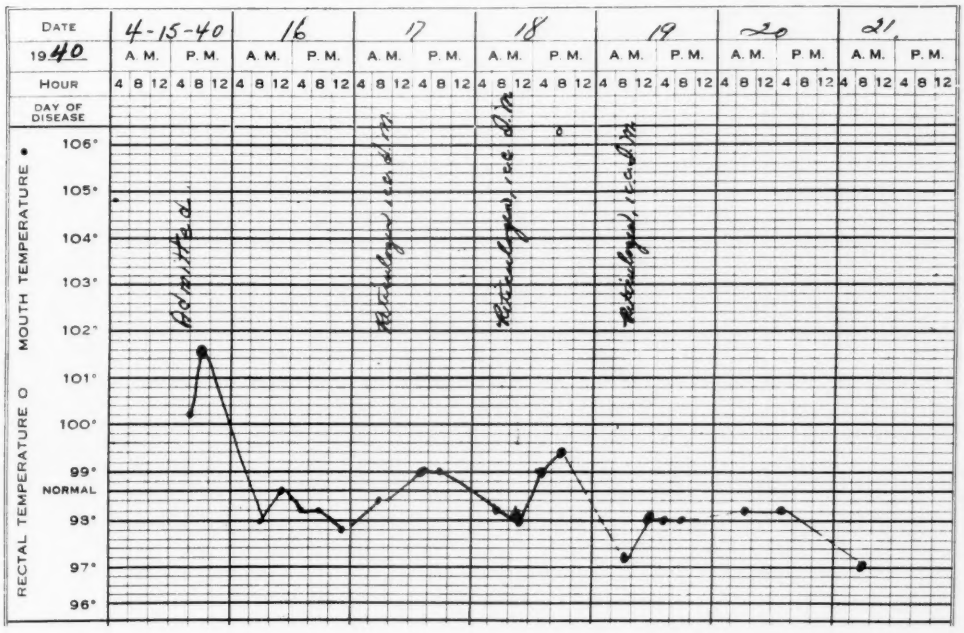

Fig. 2.—Temperature chart.

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2. Prompt cure was obtained by sulfapyridine therapy.

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LEFT RENAL AGENESIS, TRUE UNICORNUATE UTERUS, AND TOTAL ABSENCE OF LEFT BROAD LIGAMENT, ROUND LIGAMENT, SALPINX, AND OVARY*

G. A. Varino, M.D., and W. D. Beacham, M.D., New Orleans, La.

(From the Departments of Gynecology and Obstetrics, Tulane University and Charity Hospital of Louisiana at New Orleans)

Less than thirty cases of true unicornuate uterus with unilateral renal agenesis can be found in the available literature. Delaginiere,[1] Pestalozza,[2] Urban,[3] and Duncan[4] reported one case each in which the Fallopian tube and ovary were likewise absent. The salpinx, ovary, and almost all of the broad ligament were missing in a case described by Guizetti and Pariset[5] in 1911. McCrae,[6] Tschischtowitsch,[7] and Guthrie and Wilson[8] recorded a total of three instances in which the tube, ovary, and all of the broad ligament were absent. The only case presenting unicornuate uterus with complete unilateral absence of broad and round ligaments, tube, ovary, ureter, and kidney, which we have been able to find in the literature is that reported by Dannreuther[9] in 1923. The case which we are now submitting is identical to his even to the side of the anomaly but differs in that the patient had a cystic right ovary and had borne two full-term living infants.

Mrs. Y. R., white, housewife, aged 27 years, gravida ii, para ii, native of Louisiana, born of French parents, was admitted to the Charity Hospital (U. H. No. T-38-76722) on Nov. 24, 1938, complaining of "pain in the lower abdomen." The onset of her complaint dated to September, 1937, shortly after the birth of her second full-term living infant. The pain manifested itself as a "dragging sensation" in the pelvis and was frequently associated with a "feeling of pressure on the rectum." It was exaggerated by exertion and was sometimes accompanied by lumbosacral backache. Infrequently, nausea and vomiting occurred. A slight leucorrhea, presenting itself after delivery of her first baby, became very profuse, thick, and somewhat malodorous after normal termination of her second pregnancy. Local

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cervical treatment in the Charity Hospital clinic proved effective only at times, and the cervical discharge was one of the major reasons that she applied for admission to the hospital.

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Fig. 1.—Right renal pelvis and calyces are well filled ten minutes after the intravenous injection of 20 c.c. of diodrast.

and the history is negative for hematuria, passage of stone, nocturia, pyuria, and incontinence of urine even upon coughing or sneezing. She stated that her urine had been examined several times without any abnormalities being found. Review of organic systems disclosed nothing of note, and her past history was irrelevant except for an uncomplicated appendectomy in 1921. Family history disclosed nothing of importance.

The patient was a well-nourished, apparently well-developed, highly cooperative, ambulatory, afebrile, intelligent person, whose blood pressure and other physical

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mitted to the hospital for cesarean section. A classical section was done so as to avoid dissemination of tumor cells. A 6-pound 3-ounce male infant was delivered in good condition. The postoperative course was afebrile and the mother and baby were discharged on June 26, 1939.

The patient was readmitted on Oct. 4, 1939, for radical groin dissection. The lapse of time between the cesarean section and the groin dissection was much longer than originally planned because the patient refused to come in for operation. However, on Oct. 6, 1939, under gas-ether anesthesia, the femoral and inguinal glands on the left side were radically excised. Because of the length of this procedure only one side was done at that time. The right groin was dissected on Oct. 16, 1939. The pathologic report on the tissue removed showed no evidence of malignancy and the diagnosis of chronic lymphadenitis was made.

The period of convalescence was complicated by the filling of the dead space in the right groin with a serosanguineous sterile fluid which required repeated aspiration. On Nov. 14, 1939, the patient was discharged and referred back to the Tumor Clinic.

X-ray therapy was begun on Nov. 30, 1939, and completed Dec. 14, 1939. A total of 1400 r. units was given through 15 by 15 cm. ports to each groin, and a total of 1200 r. units was given directly to the perineum through a 10 by 10 cm. port. The factors were 200 K.V.; 15 MA; T.S.D.—50 cm.; 1 mm. Thoreus filter.

The patient was again hospitalized on Dec. 18, 1939, for incision and drainage of a subcutaneous abscess which had developed in the region of the right groin dissection. She also had a low-grade thrombophlebitis and cellulitis of the right leg and foot. After drainage of the abscess and conservative therapy to the leg, she convalesced rapidly and was discharged on Jan. 19, 1940. At the present time (after seventeen months), the wound in the groin is completely healed and the patient is in excellent health. No evidence of local recurrence or distant metastasis of the carcinoma can be found.

SUMMARY

Six cases of primary epidermoid carcinoma of the external genitalia complicating pregnancy, including the present report, have been recorded in the literature. Four had their primary site of origin in the vagina. Three of these ended fatally in a remarkably short time, the fourth patient was alive six weeks post partum. The final course is not known since the follow-up is incomplete. Two cases were primary squamous cell carcinoma of the vulva and were treated in a similar, though quite independent, manner. Both patients at the present writing are alive and well, one after a period of five years, the other after seventeen months.

The treatment of all operable carcinomas of the vulva is vulvectomy with complete bilateral inguinal dissection. This procedure must be tempered to fit the individual case when accompanied by pregnancy. The results of surgery for this condition are highly favorable. Taussig[9] reported 20.4 per cent and Stoeckel[10] a 31.2 per cent five-year cure rate. However, it is important to remember that these cases were not complicated by co-existing pregnancy.

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Previous History.—Onset of menses at 14 years, with five-day periods of normal flow, occurring regularly every twenty-eight days. No menorrhagia, metrorrhagia, or dysmenorrhea prior to or since marriage. During her four years of marital life she has been delivered of two normal males. There had been no dyspareunia. She does not remember ever having any frequency of, or burning upon, micturition,

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the tumor mass, cesarean section, bilateral radical groin dissection, post-op. x-ray therapy.

3. Five other cases of carcinoma of the external genitalia complicating pregnancy in young women were collected from the literature. We agree with Russell that more cases must have occurred but were not reported.

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PRIMARY PNEUMOCOCCIC PELVIC PERITONITIS IN AN ADULT; PROMPT CURE BY SULFAPYRIDINE THERAPY

W. Duncan Owens, M.D., Miami Beach, Fla.
(From the Department of Surgery, St. Francis Hospital)

PRIMARY peritonitis due to the pneumococcus in an adult is not frequent; when it is confined to the pelvis, it is rare indeed. In 1938 Nuckols and Hertig[1] were able to collect from the literature but 77 cases; only 23 of these were not associated with a recent obstetric episode. In 1940, Bennett and Mengert[2] added 2 cases. In 1939, Barnett, Hartmann, Perley and Ruhoff[3] reported the use of "sulfapyridine" in the treatment of pneumococcic peritonitis in 5 children, all of whom recovered. In 1939, Ladd, Botsford and Curnen[4] recommended the use of "sulfapyridine" in pneumococcic peritonitis in infants and children. A search of the literature has not revealed a report of the use of "sulfapyridine" in primary pneumococcic peritonitis, pelvic or general, in an adult.

CASE REPORT

On April 15, 1940, Mrs. E. N., a graduate nurse, aged 41 years, widow for two years, presented herself at the office. Four days previously she had first noted a profuse, irritating, greenish vaginal discharge which was accompanied by a mild diarrhea and occasional cramps in the lower abdomen. Two days later pain appeared in both lower quadrants of the abdomen, and diarrhea and cramps became worse. The same day for the first time, she had a temperature of 101° F. and

nausea, but no vomiting occurred. She had been on duty for over fourteen months with an aged male patient with a draining empyema cavity from which pneumococci and tubercle bacilli were said to have been recovered elsewhere. Except for an appendectomy about twenty years ago she had been well all her life; had never been pregnant and menstrual history had been unremarkable until four months previously, when a mild menometrorrhagia appeared and has continued. Last menstrual period was fourteen days before present illness. Coitus for the past two years was denied. There had been no cough or other respiratory difficulty. Examination revealed: Temperature, 100.4° F.; pulse, 96; respirations, 20; nose and throat clear and without discharge; lungs without evidence of pathology; abdomen, an old right rectus incisional scar, tenderness 1-plus in both lower quadrants, no spasticity or rebound pain; pelvis, a profuse, greenish yellow, blood-streaked discharge from the cervix, pain 4-plus upon motion of the cervix, especially upon lifting it forward, pain 3-plus to 4-plus throughout the pelvis, with generalized thickening but no masses, palpation difficult and unsatisfactory due to extreme pain. Smear made from the cervical discharge (Gram stain) showed many pus cells, polymorphonuclears; many red blood cells; many gram-positive extra-

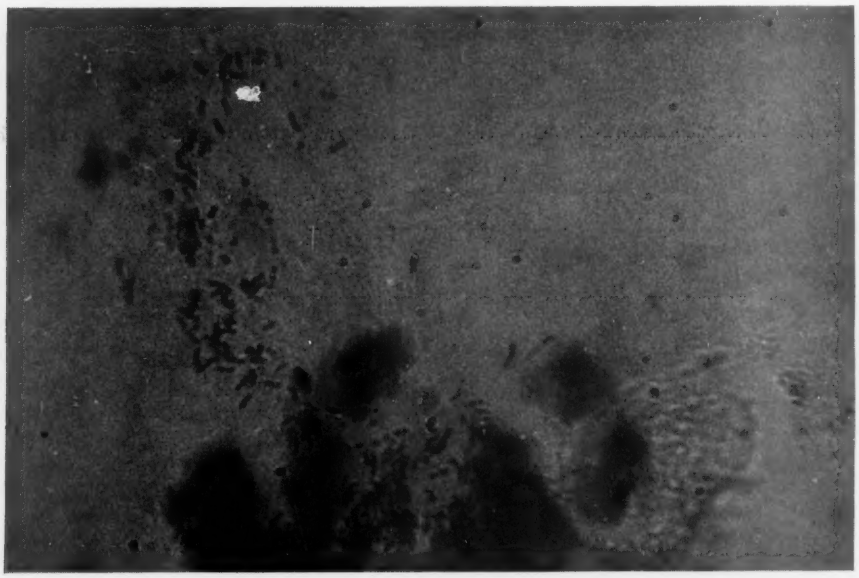
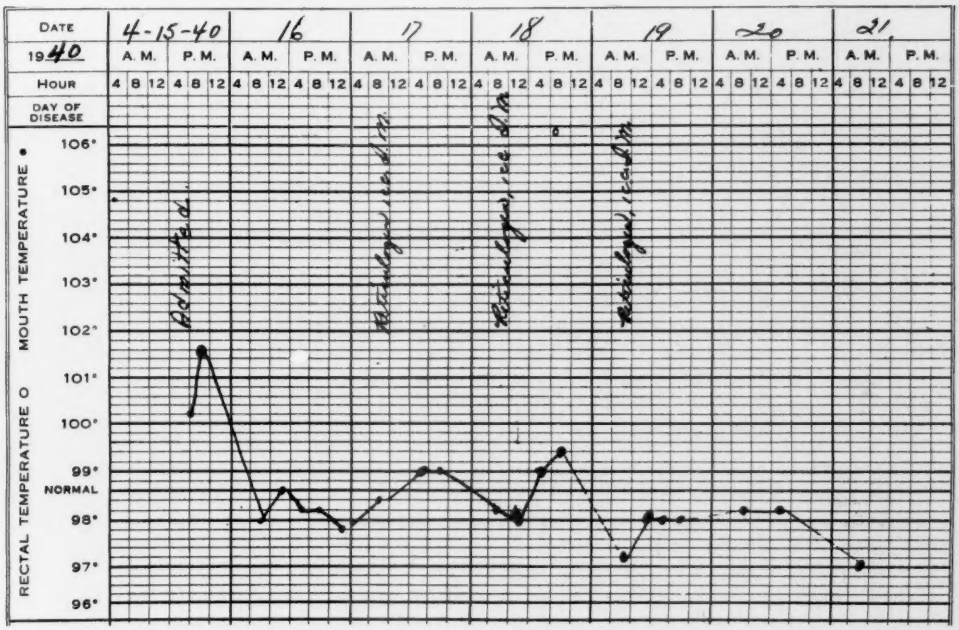


Fig. 1.—Photomicrograph of cervical smear, showing gram-positive extracellular encapsulated diplococci.

cellular encapsulated diplococci resembling pneumococci; no intracellular organisms. Material for typing and culture was obtained from the cervix upon sterile swabs and later taken to the hospital where it was reported they had dried to such extent that typing was impossible; culture was made, nevertheless, but showed no growth. Complete blood count showed hemoglobin 60 per cent; red blood cells 3,280,000; white blood cells 12,950; Schilling differential, neutrophiles 79 per cent, segmenteds 49 per cent, band forms 29 per cent, juvenile forms 1 per cent, lymphocytes 21 per cent. Early primary pneumococcic pelvic peritonitis was diagnosed, and she was admitted to St. Francis Hospital, admission No. 19233, at 6 P.M., April 15, 1940, where chest films showed no pathology. Sulfapyridine therapy was begun at once: 2 Gm. at each of the first 2 doses, four hours apart; then 1 Gm. every four hours, awakened if necessary; soda bicarbonate 4 Gm. with each of the first 3 doses of "sulfapyridine," then 3 times a day; fluids only as desired for the first eighteen hours, then to be forced to 3000 c.c. per twenty-four hours. pH of the urine was done at each voiding and remained at 7.5 throughout, otherwise normal. Nausea

was experienced the following day, April 16, and that evening she was given intravenously 500 c.c. of one-sixth molar sodium lactate solution and 500 c.c. of citrated blood. The next day, April 17, "sulfapyridine" concentration in the blood was 6.65 and that afternoon the dosage was reduced to 1.5 Gm. every eight hours for 3 doses, when it was discontinued. Total amount of "sulfapyridine" given: 16.5 Gm. in 13 doses, from April 15, 7 P.M. to April 18, 8 A.M. Only liquids, but including gelatin mixture, were allowed through April 19. Because of the secondary anemia, 1 c.c. of "reticulogen," was given each day of April 17, 18, 19. Temperature fell to normal on April 16 and, except for a slight rise on April 18, remained down; pulse and respiration came to normal on April 16 and remained so.

On April 18 complete blood count showed hemoglobin 78 per cent; red blood cells 4,020,000; white blood cells 5,000; Schilling differential, neutrophiles 71 per cent, segmenteds 58 per cent, band forms 12 per cent, juvenile forms 1 per cent, eosinophiles 3 per cent, lymphocytes 26 per cent. Blood culture taken on April



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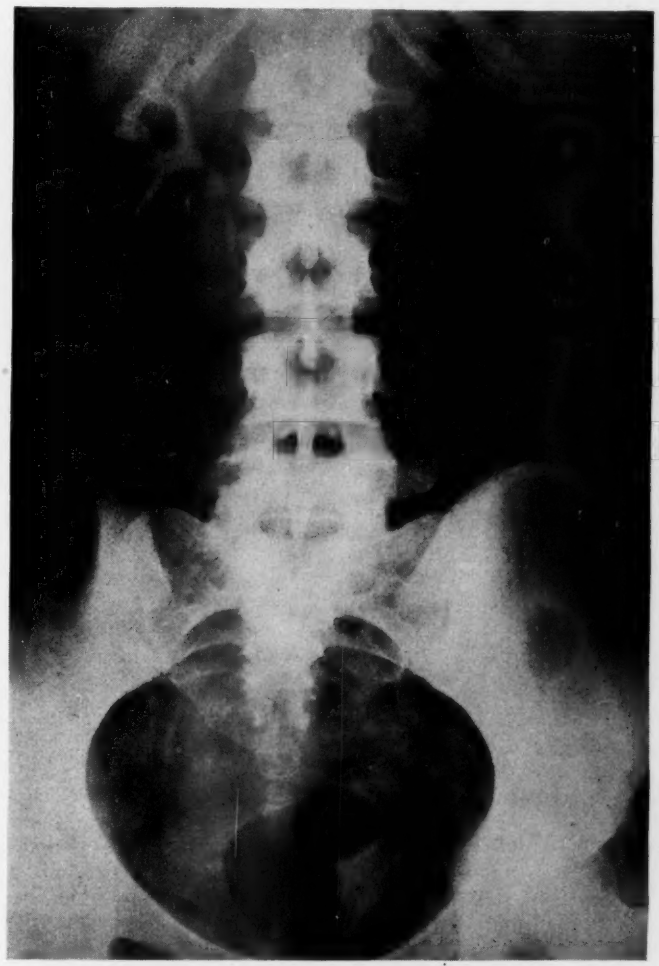

Fig. 1.—Right renal pelvis and calyces are well filled ten minutes after the intravenous injection of 20 c.c. of diodrast.

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The patient was a well-nourished, apparently well-developed, highly cooperative, ambulatory, afebrile, intelligent person, whose blood pressure and other physical

findings, excluding those of the internal genitalia, were normal. Vaginal examination disclosed moderate relaxation of the perineum with a slight rectocele and a markedly lacerated, cystic, hypertrophied cervix. The uterus appeared to be of normal size, was retrocessed, second degree retroverted, and freely movable without pain. Traction on the cervix, however, did give rise to an expression of considerable discomfort. The right ovary was considerably enlarged and was in the culdesac. Neither tube nor the left ovary was palpable.

The studies of the blood and urine being normal, the patient was subjected to operation on Nov. 28, 1938, under ethylene anesthesia. After dilatation of the cervical canal, a Sturmdorf amputation of the cervix and Hegar perineorrhaphy were performed. The patient was then placed in a Trendelenburg position and the abdomen opened through a Pfannensteil incision. Palpation and inspection revealed the presence of a cystic prolapsed right ovary with complete absence of the left Fallopian tube, ovary, round and broad ligaments. The left iliac fossa

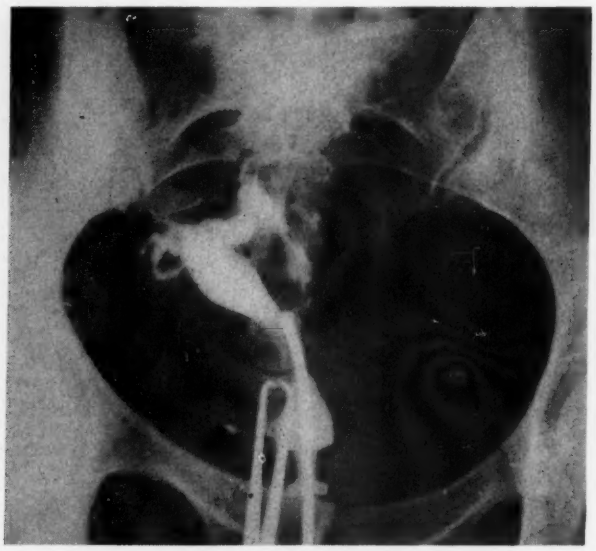

Fig. 2.—Hysterosalpingogram proves the right tube to be patent. There is dextroversion of the uterus. This roentgenogram was taken after 10 c.c. of 40 per cent skiodan solution had been injected into the uterine cavity.

was occupied by the sigmoid and rectum, and the vesical peritoneum followed the left margin of the uterus down to the vault of the vagina where it fused with the parietal peritoneum. The ovary being about 6 cm. in its greatest diameter, it was deemed advisable to resect the cystic portion. The uterosacral ligaments were then shortened after the technique of Kelly, and the right round ligament was plicated. Further support to the right ovary was obtained by shortening the infundibulopelvic ligament. The uterus was of the true unicornuate type, and its color and consistency were good. The right ureter was demonstrable, but the left was missing. No attempt was made to palpate the kidney areas due to the type of incision. The abdomen was closed in layers with absorbable material, and she made an uneventful recovery. An intravenous urogram was made to prove absence of left kidney. As shown by Fig. 1, the pelvis and calyces of the right kidney are well filled ten minutes after the intravenous injection of 20 c.c. of diodrast. No evidence of a kidney or ureter is seen on the left side in any of the three skiagrams obtained at 10-, 30-, and 60-minute intervals.

Although the patient attended the clinic subsequently, it was not until Jan. 24, 1940, that she consented to submit to cystoscopic examination and pyelography. On that date, a No. 24 Fr. Brown-Buerger cystoscope was introduced into the bladder with ease. Clear straw-colored urine was obtained. The bladder capacity was

TABLE I.—DATA ON CASES OF TRUE UNICORNUATE UTERUS WITH UNILATERAL RENAL AGENESIS (AFTER SHUMACKER[10])

CASE	AUTHOR	UTERUS UNICORNIS	RENAL AGENESIS	URETER ABSENT	ADNEXA ON DEVELOPED SIDE	ADNEXA ON DEFECTIVE SIDE	AGE
1	Puech (1885)	R	L			Ovary in lumbar region; round ligament unconnected with uterus.	15 days
2	Rokitansky	L	R				76 yr.
3	Rokitansky	L	R				
4	Paltauf (1885)	L	R	R	Normal	Ovary long, in lumbar region; ovarian ligament extending toward inguinal ring; only ostial end of tube and round ligament present.	61 yr.
5	Winckel (1890)	R	L	L	Normal	Round ligament absent.	
6	Winckel (1890)	L	R	R	Normal	Ovary and tube solid and rudimentary; broad ligament absent.	
7	Brackenbury (1891)	R	L	L	Normal	Small rudimentary ovary above pelvic brim; no tube; broad and round ligaments rudimentary.	26 yr.
8	Naumann	R	L	L			12 hr.
9	Delaginiere	L	R			Tube and ovary absent.	
10	Pestalozza	L	R	R		Tube and ovary absent.	
11	Urban (1899)	L	R			Tube and ovary absent.	
12	Alglave (1905)	?	?			Ectopic ovary.	40 yr.
13	McCrae (1908)	R	L	L		Tube, ovary and broad ligament absent.	
14	Tschischtowitsch (1908)	R	L			Tube, ovary and broad ligament absent.	
15	Guthrie and Wilson (1909)	R	L	L	Cystic ovary	Tube, ovary and broad ligament absent.	30 yr.
16	Guizetti and Pariset (1911)	R	L	L	Normal	Tube, ovary and almost all broad ligament absent; round ligament attached to cervix.	Term Fetus
17	Guizetti and Pariset	R	L	L	Normal	Ovary and ostial end of tube 1.5 cm. long; rudimentary broad ligament; round ligament attached to cervix.	11 mo.
18	Guizetti and Pariset	R	L		Ovary 9 cm. long	Ovary 6 cm. long; only ostial end of tube present.	44 yr.
19	Guizetti and Pariset	R	L	L	Normal	Ovary and ostial end of tube in inguinal hernia; only lower half of broad ligament present; round ligament attached to cervix.	43 yr.
20	Guizetti and Pariset	R	L	L	Ovary 2 cm. long	Ovary 2.3 cm. long; only ostial end of tube present; only lower portion of broad ligament present; round ligament attached to cervix.	56 yr.
21	Boehme (1912)	R	L	L		Ovary in front of internal inguinal ring.	
22	Rosenthal (1913)	R	L			Ectopic ovary and tube.	
23	Oehler (1914)	R	L	L	Normal	Atrophic tube and ovary lying in hernial sac without connection to uterus; vessels from aorta and vena cava; broad and round ligaments absent.	59 yr.
24	Schilling (1917)	L	R	R	Ectopic ovary	Ovary long; incompletely descended; only ostial end of tube present; ovarian ligament and mesosalpinx fused with peritoneum of processus vaginalis; round ligament rudimentary.	1 day
25	Schilling	L	R	R	Normal	Ovary above linea innominata; only ostial end of tube present.	2½ days
26	Dannreuther (1923)	R	L	L	Normal	Ovary, tube, round and broad ligaments absent.	25 yr.
27	Duncan (1933)	R	L	L		Ovary and tube absent.	26 yr.
28	Shumacker (1938)	L	R	R		Ectopic ovary and tube; only ostial end of tube present; no broad ligament.	13 yr.
29	Varino and Beacham (1940)	R	L	L	Cystic ovary	Ovary, tube, broad and round ligaments absent.	27 yr.

within normal limits. There was no sign of a left ureteral orifice and no indication of an interureteric ridge. The vesical mucous membrane was normal, and there were no calculi, newgrowths, diverticula, or ulcers. The orifice of the right ureter was plainly visible. A No. 5 olivary radio-opaque catheter was introduced and passed into the right renal pelvis without any difficulty. Six cubic centimeters of clear urine were obtained. Five cubic centimeters of indigo carmine solution were administered intravenously and appeared in the urine in three and one-half minutes, being excellently concentrated in four and one-half minutes. Again inspection failed to reveal any indication of a left ureter. Twelve cubic centimeters of 40 per cent skiodan solution were injected and a pyelogram obtained. The right kidney showed evidence of compensatory hypertrophy and its pelvis and calyces were very slightly dilated. The renal pelvis was at the level of the lower border or the second lumbar vertebra. Both psoas shadows are visualized and there is no evidence of a kidney on the left. The patient was placed in an upright position and the ureteral catheter removed. The resulting pyelogram showed that the kidney descended to the lower border of the third lumbar vertebra, and the ureter could be traced. A week later, the patient returned for hysterosalpingography. Five cubic centimeters of 40 per cent skiodan solution were injected into the uterine cavity. The hysterogram was consistent with unicornuate uterus. Five additional cubic centimeters were injected and the hysterosalpingogram (Fig. 2) obtained. Dr. E. W. Brown, of the Charity Hospital X-ray Department, reported: "Views of the pelvis after injection of skiodan confirm the diagnosis of a unicornuate uterus. The latter is well visualized and the tube is patent." Study of the urine obtained at the time of cystoscopy was reported by Dr. Geo. Fasting as follows: "Bladder specimen: sediment negative, culture negative; right kidney specimen: many red blood cells and renal cells, culture negative."

Shumacker[10] has so thoroughly presented the subject of congenital anomalies of the genitalia associated with unilateral renal agenesis that a review of the literature and discussion of embryology here would be superfluous.

SUMMARY

Less than 30 cases of true unicornuate uterus with unilateral renal agenesis have been reported.

Only one case of true unicornuate uterus with unilateral total absence of broad and round ligaments, salpinx, ovary, ureter, and kidney was recorded in the literature prior to this communication.

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Escomez, Edmundo: The Ovary of Lina Medina (The Youngest Mother in the World), Presse méd. **47:** 1648, 1939.

The author describes the ovarian tissue containing the corpus luteum verum removed by the surgeon at the time of cesarean section upon Lina Medina, the five-year-old Peruvian mother. The ovary presented all the histologic characteristics of full maturity. Four fine photomicrographs are included in the article.

CLAIR E. FOLSOME.

THE ENDOMETRIAL BIOPSY IN EARLY EXTRAUTERINE PREGNANCY

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THE endometrial suction biopsy is now an accepted diagnostic procedure. The histologic findings serve as an important guide to estimate the degree of both follicle and corpus luteum activity. Sturgis[1] has recently called attention to the importance of recognizing the characteristic glandular pattern seen in early pregnancy. In addition to the decidual changes of the stroma, stress is placed upon the appearance of the swollen epithelial cells which form the glands. They balloon out into the lumen with a free edge distinct and clear-cut, resembling exaggerated goblet cells. He concludes: "The characteristic glandular response described represents an increase in function consistent with early pregnancy."

The diagnosis of early extrauterine pregnancy still remains a difficult clinical problem. We rely upon a careful history, a painstaking physical examination, complete blood count, Aschheim-Zondek test, and in some instances, pelvic puncture. However, notwithstanding the attempts to establish a definite diagnosis, it is not uncommon to have a case of early ectopic pregnancy rupture while still under observation. Therefore, any further means of confirming this diagnosis may prove invaluable to the patient.

Suction endometrial biopsy was utilized in two cases of suspected extrauterine pregnancy. The histologic findings obtained were definite enough to warrant the diagnosis of early gestation. The cases are reported in detail as follows:

CASE 1.—A. J., aged 28 years, single, first seen Feb. 21, 1940, had been spotting for two weeks. Last period occurred Jan. 1, 1940. During the latter part of January the patient had low abdominal pain, intermittent in character, but not severe enough to cause confinement to bed. When she presented herself at the clinic as an ambulatory case, she did not look acutely ill. There was a blood-stained vaginal discharge. Bimanual examination disclosed a soft cervix, a small, rather firm uterus, and a mass, the size of a plum, in the right fornix. This mass was soft in consistency and moderately tender. Movement of the cervix caused no pain. A complete blood count showed: red blood cells, 4,250,000; white blood cells, 6,450; Hb, 80 per cent; polymorphonuclears, 65 per cent; lymphocytes, 32 per cent; eosinophiles, 2 per cent; monocytes, 1 per cent. Sedimentation rate was 20 mm. first hour. An endometrial biopsy was taken, from which a frozen section was made and examined by Dr. Grete Stohr, who submitted the following report:

The fragments are of appreciable size; the glands are densely distributed. Their trans-sections are wide and their lumina are serrated. The epithelial cells are broad, more square than columnar. Their apical portion is dome-shaped with clear protoplasm bulging into the lumen of the gland, or they are flat with frayed inner edges, with large, pale nuclei. In other, less frequent instances, they are corkscrew-shaped with folded columnar epithelium. The stroma is composed in

broad fields of a compact layer showing distinct changes of a decidual reaction. Chorionic elements are not encountered, neither as chorionic villi nor as chorionic cells.

Diagnosis.—Decidua of early pregnancy (suggestive of ectopic pregnancy) (Figs. 1 and 2).

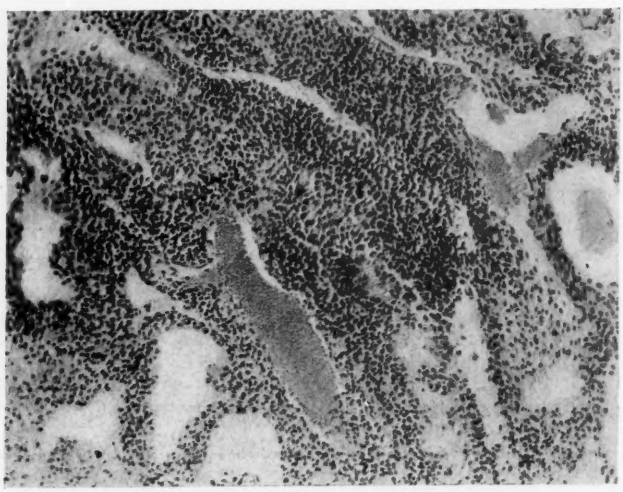

Fig. 1.—Endometrial biopsy showing decidua spongiosa.

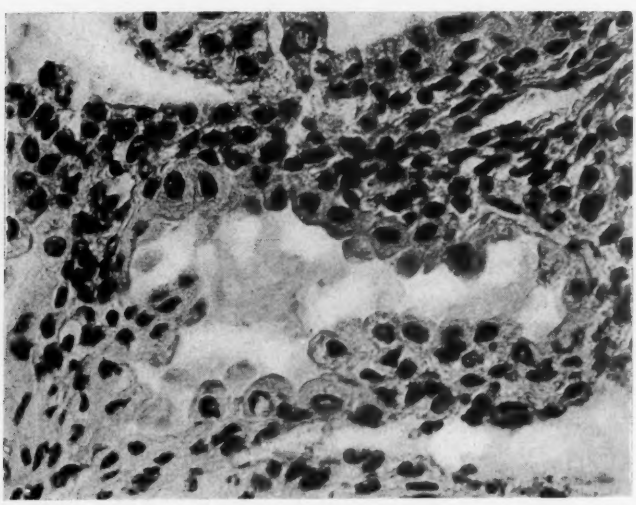

Fig. 2.—Detail of endometrial gland showing characteristic scalloped outline and dome-shaped cells.

The elapsed time between taking the endometrial biopsy and receiving the report of the frozen section was thirty minutes. Following this report, the patient was immediately hospitalized and prepared for operation.

At the time of operation, the uterus was found to be normal in size, but soft in consistency. A mass 10 cm. in length and 4 cm. in width was found, consisting of a distended right tube, which was firm and hemorrhagic. There was no free blood in the pelvic cavity. The left tube showed evidence of chronic inflammatory disease.

Pathologic Examination.—The right tube was transformed into an ovoid structure 9 cm. long and 5 cm. at its widest diameter. Cross section through the tube showed a partially formed placenta which penetrated through the entire thickness of the wall. The abdominal ostium of the tube presented a wide opening 2 cm. in diameter. The umbilical cord emerged from this opening; it was attached to an embryo 70 mm. in length, found just outside the ostium.

Microscopic section of the wall of the right tube showed partial or complete consumption of the tissues by implantation of the placenta, while other portions revealed a well-preserved tubal wall (Fig. 3).

Diagnosis.—Right tubal pregnancy and tubal abortion.

The patient made an uneventful recovery following her operation, and was discharged from the hospital in good condition.

CASE 2.—M. H., aged 32 years, married, was first seen March 24, 1940, complaining of lower abdominal pain. Last period occurred Feb. 22, 1940. On March 22, the patient had lower abdominal pain, which subsided on application of heat. The following day, the patient was seized with intense abdominal pain which caused a

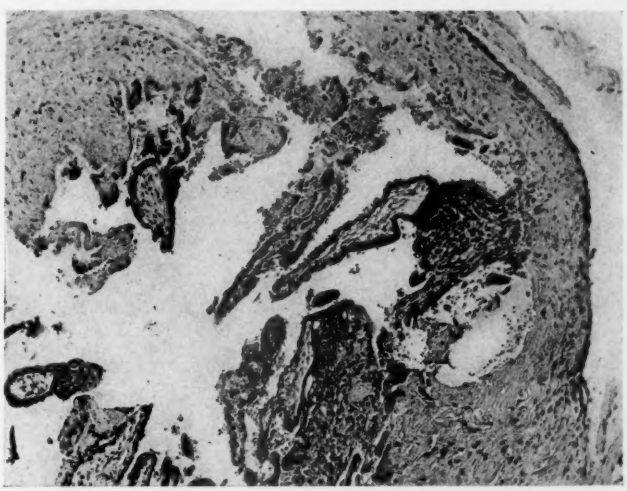

Fig. 3.—Section of tube showing implanted chorionic villi.

restless night. The pain was continuous, accompanied by slight vomiting. The pain became localized in the left lower quadrant. Concomitant with the onset of pain, there appeared a dark reddish-brown vaginal discharge which did not resemble a normal period.

Past History.—Operation in June, 1937, for endometriosis, with removal of right adnexa. She had been married for ten years, but had never been pregnant. Upon physical examination, the abdomen revealed no tenderness or rigidity. Upon vaginal examination, there was a brownish discharge. The cervix was not tender upon motion. The uterus was small, retroplaced. In the left fornix was a tender mass the size of a hen's egg, rather hard in its lower aspect, and softer in its upper portion.

Complete blood count: Red blood cells, 3,230,000; white blood cells, 6,650; polymorphonuclears, 68 per cent; lymphocytes, 32 per cent; Hb, 67 per cent. Sedimentation rate, 32 mm. first hour.

Endometrial suction biopsy was taken and the following report was submitted by Dr. Grete Stohr:

The fragments of endometrium were examined in frozen section. They are built of typical decidual stroma cells in which large tortuous, greatly serrated glands are embedded. On cross section, they have the characteristic rosette shape of the actively functioning gland. The epithelial cells are generally of a medium tall

columnar type, alternating with stretches of lower cells, according to their location at the top or bottom of infolding crests. Nuclei are near the base of the cells; the entire cell substance is finely vacuolated, and the clear apical portion of the cells, when conformed to a row, produces a transparent scalloped border against the lumen of the gland.

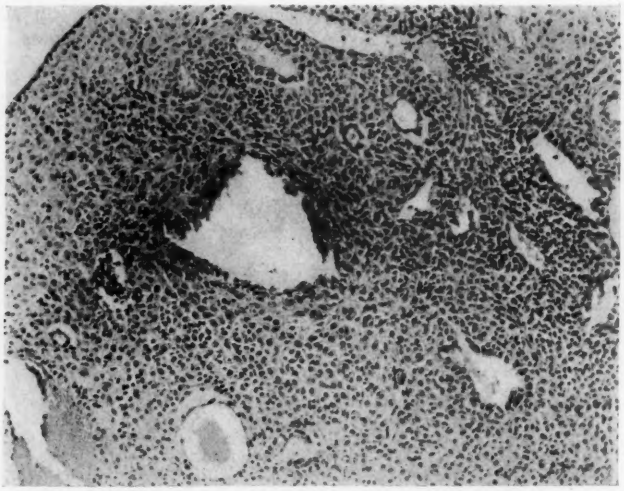

Fig. 4.—Endometrial biopsy; compact decidua; large stroma cells.

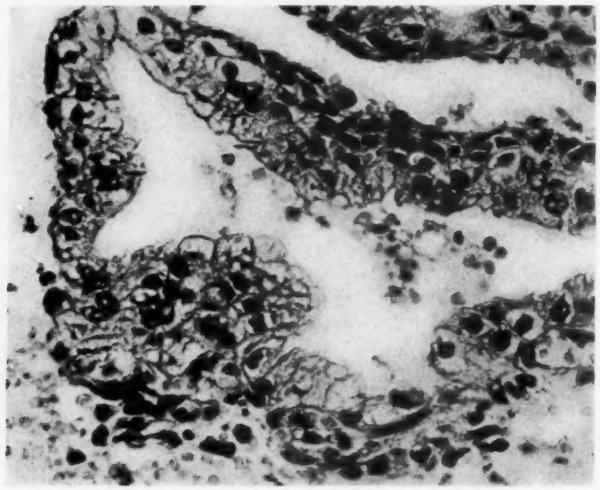

Fig. 5.—Characteristic gland with cells showing clear protoplasm and dome-shaped contours.

Diagnosis.—Decidua of pregnancy. Chorionic elements not found. (Indicative of ectopic pregnancy.) (Figs. 4 and 5.)

Laparotomy was performed immediately upon the report of the endometrial biopsy.

At operation, the uterus was small and appeared to be normal. The right adnexa were missing. On the left side there was a mass the size of a small orange. This mass consisted of an adherent left ovary, containing a large corpus luteum. Sur-

mounting the ovary was a dilated tube about 8 cm. long and 5 cm. wide. The tube was filled with clotted blood. The clinical diagnosis was tubal abortion.

Pathologic Examination.—The tube, which was surrounded by large, loose and adherent blood coagula, was examined in many sections. In the majority the mucosa was partly reduced to a few atrophic folds; in other instances, folds were hypertrophic, congested, but without any evidence of inflammation; the muscle layers were thin and likewise hyperemic. In one of the sections, approximately half of the tube wall formed the site of implantation of compact masses of trophoblast cells and chorionic villi, which had penetrated and consumed this portion of the tubal wall except for the most peripheral thin layer of subserous connective tissue. Here, occasionally short fragments of the muscle tissue were preserved. A complete rupture of the wall was not apparent in successive sections. The chorionic tissue was well-preserved without any evidence of disintegration. Diagnosis: Early tubal pregnancy (not ruptured) (Fig. 6).

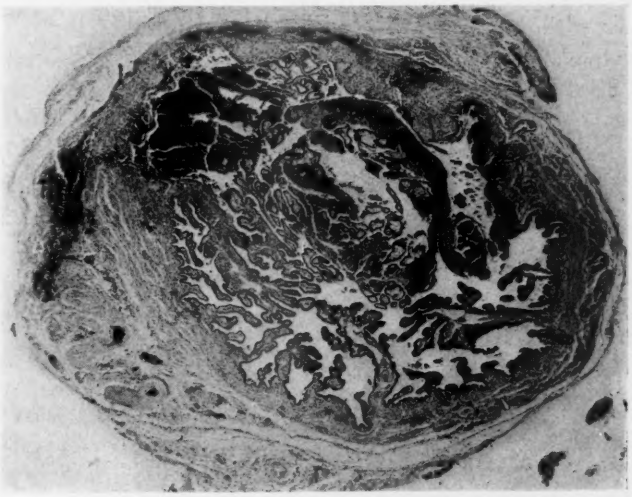

Fig. 6.—Cross section of tube from site of placental implantation.

DISCUSSION

Endometrial biopsy, in two cases of early tubal pregnancy, proved a valuable aid in establishing a diagnosis. It must be emphasized that the biopsy should be performed at the hospital under strict aseptic technique, and the patient prepared for immediate operation if rupture should occur while manipulating the uterus. In our two cases, there was no ill effect whatsoever, from the biopsy procedure. In early extrauterine pregnancy, the endometrium, stimulated by progesterone, presents the characteristic changes in both the stroma and glands. Later on, if death of the fetus occurs, the decidua may be cast off, with subsequent change of the endometrial picture. This factor should be kept in mind in the interpretation of the histologic pattern of the endometrium.

Goldblatt and Schwartz[2] correlated the Friedman test and the phase of the endometrium in ectopic pregnancy. They found that no patient with a negative Friedman test had a decidual reaction at the time of curettage; and conversely, no patient

with uterine decidua had a negative Friedman test. They state there is a close but not perfect relationship between the result of the Friedman test and the state of preservation of the chorionic villi.

Recently, TeLinde and Henriksen[3] have reported a number of cases with decidua-like changes in the endometrium without pregnancy. Many of these occurred in endocrine disorders in which increased progesterone activity was present. However, they state that "curettage is often of great value in the diagnosis of tubal pregnancy, but the microscopic picture must be interpreted correctly if it is to be of value."

It must be borne in mind that the endometrial study should not be regarded as the sole method of establishing the diagnosis. We must take into consideration the history and the clinical data, together with the histologic findings. Furthermore, it must be emphasized that endometrial biopsy should not be attempted if intrauterine pregnancy is suspected. Sturgis[1] performed 7 endometrial biopsies in intrauterine pregnancies without interrupting gestation. In our series[4] of 500 endometrial biopsies, we encountered one instance of intrauterine pregnancy in a patient with functional uterine bleeding. The pregnancy was not interrupted, and the patient was delivered of a normal full-term baby. However, unless the history and physical findings are definitely suggestive of ectopic pregnancy, we feel that endometrial biopsy is unwarranted.

CONCLUSIONS

1. The characteristic picture of the endometrial stroma and glands in pregnancy can be obtained by endometrial biopsy.

2. The use of suction biopsy has proved successful in confirming a diagnosis of unruptured ectopic pregnancy in two cases.

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31 Lincoln Park

Haworth, Norah A.: Malnutrition and Debility in Puerperal Psychoses, Lancet **2:** 417, 1939.

An analysis of a series of 117 cases of mental illness arising in connection with childbirth and requiring hospitalization was made in an attempt to determine what additional precipitating factors might have been present. Seventy-two of the patients recovered; 60 had already had one or more normal confinements and 12 have had one or more confinements since discharge from the mental hospital without developing mental symptoms.

The majority of the patients were underweight and in poor physical health, and about one-fourth had been exposed to severe economic or emotional stress. The author believes that these two factors may be of great importance in precipitating the mental disturbance and that many cases could be prevented by attention to nutrition, general health, and environmental conditions early in pregnancy.

Carl P. Huber.

THE SIMULTANEOUS OCCURRENCE OF CARCINOMA AND SARCOMA IN THE SAME UTERUS

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SARCOMA of the uterus is not common, and the simultaneous occurrence of primary sarcoma and carcinoma of the uterus is even more rare. Twenty-eight cases were found in the literature, to which two case reports are here added.

A review of the literature on the coincidental existence of carcinoma and sarcoma in the same organ reveals considerable confusion in terminology. Oskar Frankl[1] emphasized the necessity for careful use of nomenclature and suggested "carcinoma sarcomatoides" for a carcinoma with the growth characteristics of a sarcoma; "carcinosarcoma" for intimate mixtures; and "sarcoma plus carcinoma" in those cases where separate tumors could clearly be demonstrated. The classification, however, has not been universally followed, and evaluation of the reported cases is difficult. Hoffman,[2] for example, has recently reported a clear-cut case of separate primary neoplasms, using the term "carcinosarcoma." In an effort to avoid this confusion an attempt has been made in this paper to include only those cases which apparently demonstrate distinct fundal primaries of differing type.

On this basis, 28 cases of separate carcinoma and sarcoma of the uterus were found in the world's literature. Major's report in 1918[3] included 12 cases, 8 carcinoma plus sarcoma, and 4 adenocarcinoma and sarcoma. In an extensive review of the literature in 1932, Warren and Gates[4] added 10 more cases of carcinoma plus sarcoma of the body of the uterus. Owen's[5] series of double malignancies in 1921 included no uterine neoplasms, while the figures of Newell[6] in 1929 are included in the Warren and Gates report. Since 1932 6 more cases have been reported,[2, 7-11] and the records of two additional patients are presented here.

CASE REPORTS

CASE 1.—The patient, V. M., was a 66-year-old white woman, para ii, who had passed through the menopause at the age of 50. Since that time, she had had irregular intervals of minimal spotting, the episodes occurring every one to three months and lasting twenty-four hours. For one month prior to reporting to the University Hospital clinic, she had also had postdouche and postcoital spotting. Three episodes of profuse bleeding during the last of August, 1939, resulted in her admittance to a local hospital, where a positive biopsy was said to have been obtained and the patient was transferred to the University Hospital Sept. 14, 1939.

Examination revealed an obese white female with a blood pressure of 210/90. Pelvic examination: The vaginal outlet was parous and showed menopausal changes. The cervix was irregular, friable, and bled easily on manipulation. There was a redundant polypoid growth extending through the cervical os. This bled profusely and was easily biopsied, large pieces of tissue coming away with a sponge forceps. Rectovaginal examination showed the uterus in the midposition, slightly larger than normal, movable, with questionable thickening in the right adnexal region.

Blood Kahn was negative. Hemoglobin 75 per cent, with a normal white count. The patient had occasional mild glycosuria while in the Hospital. The glucose tolerance curve was classified as the glycosuria of obesity type by the Diet Therapy Department.

Pathology.—The original biopsy was reported as: "Sarcoma, spindle cell, possibly a leiomyosarcoma. Numerous mitotic figures. Ulcerated surface. Nests of squamous epithelium below the surface, but no carcinoma found."

X-rays of the chest, spine, and skull were negative for evidence of metastases, and on Sept. 21, 1939, the patient was operated upon. The polypoid mass protruding through the cervix was removed and the cervix closed. At laparotomy a total hysterectomy and bilateral salpingo-oophorectomy were performed.

Pathology report on operative specimen: Gross: A uterus measuring 8 by 4 by 6 cm. with adnexa intact. There was no evidence of fibroids. On opening the uterus, multiple (about 12) polypoid structures were found arising in the fundus. The largest were about 4 cm. long and had a stalk 4 mm. in diameter. These had been hanging through the cervix, producing the lesion which was biopsied. The serosal surface of the uterus was intact. Microscopic: Advanced adenocarcinoma of the endometrium infiltrating almost through the uterine wall. The large polypoid masses arising in the fundus consisted of spindle cell sarcoma as reported in the previous biopsy. There was some proliferation of the adenocarcinoma into this (Fig. 1).

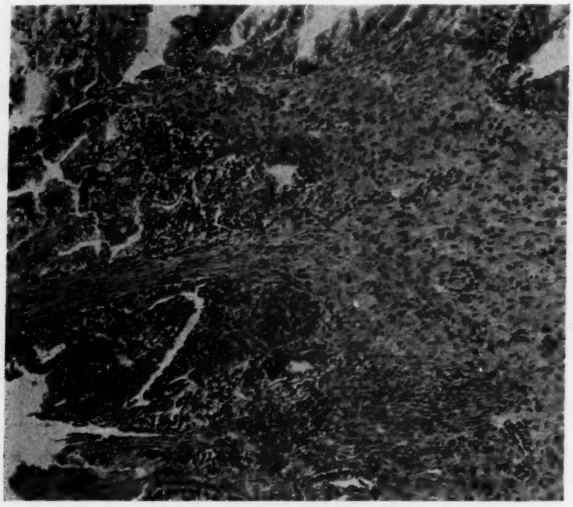

Fig. 1.—Microscopic section under low power, showing areas of mutual invasion of carcinoma and sarcoma.

The postoperative course was uneventful. The patient developed a mild urinary tract infection which was easily controlled with neoprontosil. She was allowed up on the thirteenth postoperative day. She has reported to the Clinic regularly by letter, and was last heard from in June of 1940 at which time she stated she felt well. She has not, however, returned for follow-up examination.

CASE 2.—The patient, O. Z., was a 58-year-old white nullipara who was four years postmenopausal. She was admitted to the University Hospital June 14, 1940 with a six-month history of daily vaginal spotting which had been gradually increasing. For the six months prior to the onset of bleeding, she had had a watery leucorrhea of moderate amount. Past history and family history were noncontributory.

Examination revealed a well-developed, somewhat obese white female. There was moderate emphysema of the chest; blood pressure was 160/96. The external genitalia showed menopausal atrophy. The cervix pointed posteriorly and was small and conical. The fundus of the uterus was anterior, slightly enlarged, freely movable. No adnexal pathology was palpated.

Blood Kahn was negative. Hemoglobin was 92 per cent with normal red and white counts. Urine was negative other than a rare white blood count in the microscopic sediment.

On June 18, 1940, the patient had a diagnostic dilatation and curettage and conization of the cervix. The pathology report on the curettage was: Spindle cell sarcoma of a type that could have arisen from a leiomyoma. Neoplasm cellular and rather anaplastic.

After x-rays of the chest, spine, and skull were found to be negative for any evidence of metastases, the patient was operated upon on June 21, 1940. The cervix was closed and a laparotomy performed, total hysterectomy and bilateral salpingo-oophorectomy being done. No local pelvic involvement was found, at the time of operation, and the serosal surface of the uterus was intact.

Pathologic Report.—Gross: Uterus with cervix, tubes and ovaries. "In the anterior wall of the uterus there is a large friable cellular spherical mass about 4.5 cm. in diameter which protrudes into the uterine cavity. The free portion appears necrotic. Some portions of the mass show pearly whorled appearance. There is also a 2 cm. fibroid in the anterior wall without gross evidence of degeneration."

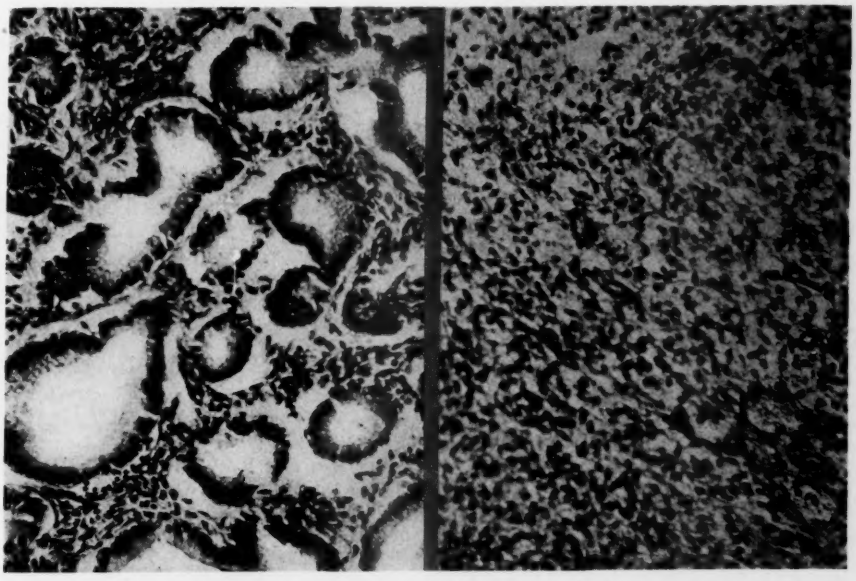

Fig. 2.—Area of adenocarcinoma (left) and sarcoma (right) from Case 2. No characteristic areas of overlapping of the two tumors were found.

Microscopic: Atrophy of the ovaries, parovarian adhesions and a small area of ovarian endometriosis. Uterus: Atrophy of the cervical glands with catarrhal cervicitis. "In addition to a large leiomyoma in the uterine wall, there is a confined malignant neoplasia of the endometrium, showing both spindle cell sarcoma as previously diagnosed and papilliferous adenocarcinoma. There is no evidence to suggest that one of these neoplastic types has been derived from the other. It seems rather that they have developed simultaneously." (Fig. 2.)

The patient's convalescence was uneventful, and she was discharged from the Hospital on her eighteenth postoperative day.

COMMENT

Statistical studies of reported cases by Warren and Gates,[4] Burke,[12] Lund,[13] and Burgher[14] have all indicated that the incidence of double primary malignancies is higher than chance would indicate. Burgher

suggested that the explanation lay in the fact that the risk of getting cancer was not spread evenly over the entire population, but over a portion of it. Cancer morbidity and mortality rates based on this reduced population figure would give a frequency of coincidental malignancy in agreement with that found in fact.

Claessan and Mathias,[15] reviewing the subject of the simultaneous occurrence of carcinoma and sarcoma in the same organ, could find a total of only 72 cases reported in the world's literature, the organ most frequently involved being the uterus.

Herxheimer[16] and Ewing[17] in discussing the pathology of carcinoma and sarcoma in the same uterus, arrive at similar theories as to possible etiology: (1) The tumors may develop simultaneously (possibly due to the same cause acting on different tissues). (2) Proliferation of the epithelium at the base of a pre-existing sarcoma, or at the point where a submucous or mural sarcoma meets the epithelial layer, may lead to development of a carcinoma. (3) The stroma of the carcinoma may undergo sarcomatous change (Herxheimer). (4) Carcinomatous changes may occur in glands of a sarcomatous polyp (Ewing). Doubtless the carcinoma sarcomatoides which Virchow described was, as he suggested, a true mixed tumor in which both epithelial and connective tissue elements were represented in the neoplastic growth. Saphir and Vass, in 1939,[18] expressed doubts that any of the then reported cases represented distinct co-existent primary neoplasms.

In both the cases here reported, however, true independent primary growths were demonstrated. While a coincidental fibroid nodule was found in the uterine wall of one uterus (Case 2), in neither patient was there definite evidence of the sarcoma's having arisen on the basis of malignant fibroid degeneration. It is interesting that in both cases the preoperative diagnosis on the basis of pathologic material was sarcoma. The coincidental existence of the carcinoma was discovered in each case after laparotomy. In both cases there was a distinct geographic separation of the two tumors in the uterus.

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LOCALIZED ENDOMETRIAL REST IN UTERINE WALL

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ADENOMYOSIS of the uterus may be conveniently divided into three types on the basis of location. The first type is the well-known adenomyosis uteri interna which arises from the basal layer of the endometrium. Various local conditions in the myometrium, particularly pregnancy and sometimes inflammation, render the uterine muscle more susceptible to invasion by the endometrial tissue in a greater or less degree, producing the typical picture of uterine glands and stroma surrounded by myometrium. In this type, it is usually possible to demonstrate an original connection between the buried glands and the basalis of the endometrium. These glands respond to hormonal stimuli much as the basal glands of the endometrium. They do not ordinarily exhibit secretory changes during the luteal phase of the cycle but may show secretory change and rarely decidual reaction during the time of pregnancy. They do not undergo menstrual necrosis. About 50 per cent of the cases of adenomyosis uteri interna are combined with cystic glandular hyperplasia of the endometrium.

The second type is the so-called adenomyosis uteri externa. Here the endometrial glands are situated on or beneath the serosal surface of the uterus, and there is no demonstrable connection with the endometrium of the uterine cavity. These glands take their origin from several sources. Ectopic endometrium may be implanted on the uterine serosa from ruptured endometrial cysts of the ovary or endometriosis of the tube. Endometrial-like glands may arise, particularly in areas of adhesions between the uterus and surrounding structures, directly by a metaplasia of the serosal epithelium. This possibility is as yet a theoretical one and difficult to prove or disprove. There is also the remote possibility that the glands may reach the serosal surface by direct extension through the entire myometrium originating from an adenomyosis uteri interna as described above.

The purpose of this paper is to discuss briefly a third or intermediate form of adenomyosis which apparently has been overlooked by most writers and to present a description of a case in point. This third type arises from aberrant portions of Müllerian epithelium which have become separated from the Müllerian ducts during the stage of development of the genital tract, resulting in the production of separate endometrial islands in the myometrium. They represent, therefore, developmental anomalies. These endometrial islands may be found in any part of the uterus but are most often found near the serosal surface, producing at times visible projections above the surface of the uterus. Some cells of the Müllerian epithelium deviate in the earliest stage of development or, perhaps more often, during the confluence of both Müllerian ducts, thus forming separate endometrial islands (Fig. 1). From these islands large

cysts with thick muscle walls may arise. The myometrium surrounding the island proliferates as it does around myomas. Robert Meyer[2] has described and collected 10 cases in fetuses and children (Fig. 1). In 7 of these cases, the island was found in the uterine fundus and in 3 cases in the cervix. Six of the 7 fundal islands were situated in the midline and all of the cervical islands were in the midline. Seven of the 10 islands were in the posterior wall and 3 in the anterior wall. These endometrial islands develop along with the normally situated endometrium. In some cases the aberrant endometrium undergoes the changes

Fig. 1.

Fig. 2.

Fig. 1.—Transverse section through the uterine fundus of a newborn child. Note the uterine cavity below and the endometrial island in the midlane of the dorsal wall.

Fig. 2.—Section through the nodule excised from a subserosal position on the left uterine wall. Note the small cavity in the shape of a cleft. The cavity is surrounded by a thick decidual layer. Surrounding this is a layer of longitudinal smooth muscle outside of which the muscle of the uterine wall is seen. Note also the scattered endometrial glands in the longitudinal muscle layer.

of the normal cycle, including menstrual necrosis. In other cases secretory changes and menstrual necrosis do not occur. One might postulate that the reason for this difference in behavior is dependent on the location of the island in the myometrium. If the aberrant endometrium is situated so as to be heavily compressed by the myometrium surrounding it, the endometrium may be prevented from reacting to hormonal influences. Decidual changes may occur during the time of pregnancy as demonstrated in our case. The island of aberrant endometrium may also act as a source for the development of an adenomyosis. The case to be described presents a minor degree of such adenomyosis (Figs. 2 and 3).

Case History.—A 29-year-old white female was admitted in the fourteenth week of her fifth pregnancy. She had a marked hypertension, and a diagnosis of chronic pyelonephritis and moderately advanced arteriolosclerosis was made. Her previous menstrual history was normal except for moderate lower abdominal cramps during the period of flow. Periods occurred every three weeks with a four- to five-day flow. It was decided that interruption of the pregnancy was indicated. An abdominal hysterotomy was carried out. At the time of operation, an elevated nodule about 3 cm. in diameter was noticed just beneath the serosa on the left uterine wall, immediately beneath the uterine end of the left tube. This felt hard on palpation, and it was thought to represent a subserous myoma. The mass was therefore excised. It was noticed, however, in the course of the dissection that the mass did not shell out as easily as might be expected.

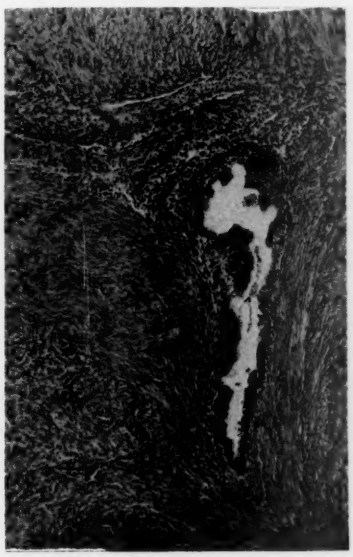

Fig. 3.

Fig. 4.

Fig. 3.—High power view of the secondary adenomyosis in the longitudinal muscle.
Fig. 4.—High power view of the stroma lining the cavity. Note the large decidual cells.

Specimen.—Gross: The operative specimen measured 3 by 2½ by 2 cm. It was irregularly rounded. In its central portion a small lumen could be seen. This lumen was lined by a thick membrane. The wall adjacent to the lumen measured 1 cm. in thickness. There was no connection between the central canal and the surface of the uterus.

Microscopic Examination: (Fig. 2.) In a section through the nodule, a small cavity in the shape of a cleft was seen. The cavity was surrounded by a thick decidual layer. The inside surface epithelium was intact and composed of a single layer of cuboidal epithelium. Only a few small glands were seen in the basal area. The stroma had undergone a marked decidual change (Fig. 4). The stroma cells were large. They had a clear cytoplasm with small dark-staining nuclei which were situated eccentrically for the most part. The reticulum was very delicate. In some areas, a small amount of old blood pigment could be seen. Surrounding the endometrium was a layer of longitudinal smooth muscle outside of which the muscle of the uterine wall was compressed to form circular layers. Occasional scattered endometrial glands and stroma had invaded the longitudinal muscle layer (Fig. 3). The myometrium was edematous throughout.

Diagnosis.—Endometrial island in the uterine wall with secondary adenomyosis and decidual reaction.

Although the finding of aberrant endometrial islands has been described by Robert Meyer,[1, 2] the English literature contains very little reference to such occurrences. Loyer[3] reports the finding of an "interstitial endometrioma" in a 25-year-old female. A pea-sized nodule was found in the corpus uteri on the posterior wall. On cut section a central canal was seen, radiating out from which were numerous glands morphologically similar to endometrial glands. This probably represents a case similar to ours. Robert Meyer[4] reports the finding of an endometrial rest in the midline of the posterior wall of the corpus of a six-year-old orangutan.

It is probable that a number of the cases reported in the literature as endometriomas represent aberrant islands of endometrium.

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MISSED ECTOPIC PREGNANCIES

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THE object of this paper is to stress the value of two simple procedures in preventing the tragic mistake of permitting the discharge from a hospital, of a patient who had a missed ectopic pregnancy, following a dilatation and curettage for what clinically appears to be an incomplete abortion. This error may be of greatest consequence in those hospitals in larger cities to which patients come from a distance.

Fortunately, some of these patients develop tubal rupture while still in the hospital. Such an experience four days after curettage on a patient, treated for supposed incomplete abortion, whose specimens had shown only decidual tissue, illustrates the necessity of never hurriedly discharging from the hospital a patient with these microscopic findings. If decidual tissue is found without chorionic villi, a negative Friedman test should be obtained before the patient is allowed to go home.

There seems to be some controversy in the literature regarding the association of decidual tissue with pregnancy.

Sampson[1] first pointed out that decidual change occurred in the endometrium associated with ectopic pregnancy. Willer[2] wrote that any polyp, removed as a cause of uterine bleeding, which showed decidual tissue indicated a pregnancy. A recent article by Te Linde and Henriksen[3] stated that decidual tissue does not always mean a pregnancy. Therefore, the value of the Friedman test is particularly emphasized. Moreover Te Linde and Henriksen described a case in which an early embryo was found in the tube, but there was no decidual change in the stroma of the endometrium at dilatation and curettage. Siddall and Jarvis[4] found that, when the curettage was done after ten days of bleeding, in ectopic pregnancy decidual tissue was not found in 100 per cent of the cases, and only 17.8 per cent showed decidual tissue when the bleeding persisted for more than twenty-nine days.

These facts led me to follow a further restricted policy of always obtaining a Friedman test before discharge on all unexplained bleeding in the childbearing years.

The case just referred to, as well as the experiences cited from the literature, prompted a study of the records of the Gynecological Department of Roosevelt Hospital for the past five years to determine whether this was a frequent accident. These records show:

Incomplete abortions	457
Incomplete abortions, later proved ectopic pregnancies ("missed ectopics")	4
Ectopic pregnancies	66

The four cases in which the error was made represent 0.9 per cent of patients with incomplete abortion treated during this period and 6 per cent of the cases of ectopic pregnancy.

In order to get a true value of material from curettage, 100 cases, diagnosed as incomplete abortion on discharge from the Roosevelt Hospital and proved so by clinical study at the recall clinic six weeks or two months later, were used as the basis for the study of their 100 respective endometrial slides. Of 100 clinically proved cases of incomplete abortion, the slides showed:

Slides with placental villi	75
Slides with considerable decidual tissue	21
Slides with early decidual tissue	1
Slides with slight decidual-like hypertrophy of endometrial stroma	2
Slides with only blood clot and too few cells for identification	1
	100

The following case histories include the four cases from the Roosevelt Hospital Gynecological Service and one private patient treated at the North Country Community Hospital, Glen Cove, Long Island:

CASE 1.—J. Z., a married woman of twenty-five years, was admitted on April 5, 1939, to the Roosevelt Hospital, complaining of amenorrhea and vaginal bleeding of four days' duration, her last period having occurred on the first of February. On March 27 she began to have slight spotting, and six days later there were sharp pains in both lower quadrants and continued slight spotting. Physical examination revealed a soft enlarged uterus. The cervix was slightly bluish and freely movable. The adnexa were negative. Friedman test was positive in two rabbits. Because of prolonged bleeding a dilatation and curettage were done on April 10. No adnexal mass was felt. Patient's postoperative course was normal. The patient was discharged. Pathologist's report of decidual tissue apparently was overlooked in view of the finding of a small mass of tissue during curettage, which was thought to be placental tissue. The patient was readmitted one week later with severe abdominal pain. A mass was noted in the cul-de-sac, and the Friedman test was returned strongly positive. She was operated upon and a ruptured right tubal pregnancy was found.

CASE 2.—A. R., married, aged 30, was admitted to the Roosevelt Hospital on Aug. 5, 1935, with a history almost identical with the above, except that an ectopic pregnancy was kept in mind, and the patient was allowed to go home for one week before repeating the Friedman test, as she lived adjacent to the Hospital. She was readmitted six days later, having bled steadily, saturating one or two pads daily.

Four days previous to this, she had severe cramp-like lower abdominal pain which lasted about one-half hour. On the following day this pain recurred twice. The Friedman test was again positive. At operation a small ectopic pregnancy was found in the right tube.

CASE 3.—R. F., 29-year-old white housewife, was admitted to the Roosevelt Hospital May 25, 1939, with the complaint of one month's amenorrhea, followed by four weeks' continual vaginal bleeding. Physical examination revealed the vagina bathed in blood, the uterus anterior, regular in outline, soft. The cervix was soft, boggy, and bleeding from the os. Adnexal regions were apparently normal. After forty-eight hours' observation, a dilatation and curettage were done. At this time a mass was felt in the left adnexal region, but it was decided to wait a few days and then run a Friedman test, before establishing a diagnosis of ectopic pregnancy. On the patient's third postoperative day she had exquisite pain in the left lower quadrant. On examination the abdomen was spastic, with maximum tenderness in the left lower quadrant. The left adnexal region was exquisitely tender and there was bulging in the cul-de-sac. Slides of the curettings showed only decidual tissue. The patient at operation was found to have a ruptured ectopic gestation of the left tube.

CASE 4.—J. B., aged 20, was admitted to the Roosevelt Hospital Aug. 4, 1935, complaining of vaginal bleeding of eight days' duration and lower abdominal pain of twelve hours' duration. Her course was similar to that of R. F., except that the tubal rupture occurred six days after the dilatation and curettage. Here again slides of decidual tissue only were available (which were of some value in a negative way of ruling out a postabortion parametritis).

CASE 5.—C. W., private patient, aged 32, was admitted to the North Country Community Hospital, Glen Cove, on Dec. 5, 1939, with the following history. A normal menstrual period was followed in five days by eight days of spotting about the size of a half dollar on a pad. A Friedman test was started the following day and was reported two days later as negative. The patient continued to spot for six days. At this time it was felt that the patient probably had an endometrial polyp and a dilatation and curettage were advised. Physical examination, when the patient was first seen after her eight days of spotting revealed a uterus about normal size, anterior, right ovary about the size of a small golf ball, and a small left adnexal enlargement, diagnosed as a hydrosalpinx about 2 to 3 cm. in diameter. Curettings revealed no definite polyp, but about the amount of tissue that would be obtained at this date in the patient's menstrual cycle.

In view of not finding gross pathology in the endometrial cavity, the Friedman test was repeated the day following the curettage. Two days later this was reported as positive. Inspection of the microscopic slides of the curettings showed secretory glands with a very slight decidual hypertrophy of the stroma. The patient was having no abdominal pain, and it was deemed advisable to repeat the Friedman test before deciding on operation. A repeat Friedman test was started the following morning. Thirty-six hours later the patient was taken with severe lower abdominal pain. Pelvic examination revealed a tender mass in the left adnexa. Abdominal operation revealed an ectopic pregnancy in the left tube and a cystic left ovary that was about 3 by 5 by 3 cm.

Two additional patients who were correctly operated upon for ectopic pregnancies after some time on the ward, had had criminal abortions attempted a week to ten days before admission. An admission diagnosis of a postabortion parametritis had been made.

DISCUSSION

Due to the low percentage of the "incomplete abortions" being really "ectopic pregnancies," one may rely too strongly on clinical judgment and discharge such patients. The grave consequences that may arise from allowing them to leave until the pathologic slides are checked, are apparent.

It cannot be said from this study that placental tissu will be found in all cases of true incomplete abortion and decidual tissue in all cases of ectopic pregnancies, but it does suggest the following procedure:

1. Several slides should be made of the curettings, as one section may show decidual tissue, another placental tissue.

2. The microscopic slides of all patients before discharge from the hospital should be examined and, if placental tissue is found, the diagnosis may be considered correct, although uterine and extrauterine pregnancies do coexist in rare instances. If marked decidual tissue is obtained, the chances of the case being an incomplete abortion are good, but a Friedman test should be run before allowing the patient to leave. If only slight decidual-like change is noted in the stroma, the chances of an ectopic pregnancy existing are high and a negative Friedman test must be obtained before the patient is discharged.

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PUERPERAL SEPSIS DUE TO STAPHYLOCOCCUS AUREUS TREATED SUCCESSFULLY WITH SULFAMETHYL THIAZOL

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Ever since Domagk discovered that certain compounds containing the sulfanilamide radical have a pronounced chemotherapeutic action on beta hemolytic streptococci, research workers have labored in an endeavor to find new modifications of the parent substance which shall be either less toxic or possess a greater antibacterial activity on a wider range of organisms.

Barlow* and his associates have been successful in preparing two new sulfanilamide thiazol derivatives known as "sulfathiazol" and "sulfamethyl thiazol." Like sulfanilamide, they are effective against experimental streptococcic infections, and like sulfapyridine they have a pronounced antipneumococcic action, but unlike either of these preparations, they exert a pronounced effect upon staphylococci both in vitro and in vivo. Sulfamethyl thiazol, because of its increased toxicity and the occurrence of peripheral neuritis in 1 per cent of the cases, had been recommended only in severe staphylococcic infections endangering life, such as staphylococcic septicemia, pneumonia, and meningitis. Because of this, sulfamethyl thiazol has recently been withdrawn temporarily from investigational use and only sulfathiazol is available. It is hoped that in the near future a new substance will be presented to the medical profession, having as great antibacterial action but much less toxicity than sulfamethyl thiazol.

However, a case of severe staphylococcus septicemia successfully treated with sulfamethyl thiazol before its withdrawal is herewith presented.

L. T., a 35-year-old white primipara, had been married fifteen years. Her last regular period was June 12, 1939. Her pregnancy was uncomplicated except for a threat to miscarry during the first trimester. On the night of March 16 she entered the hospital complaining of regularly recurring abdominal pains. She was examined at 1 A.M. on March 17. The baby was in R.O.P. position, estimated at 8½ pounds, head unengaged. Although she was complaining of abdominal pains, there were no palpable uterine contractions. A rectal examination done at this

*Personal communication, Winthrop Chemical Corp.

time (and this was the last internal examination) revealed a closed cervix and an unengaged head. The pelvis was thought to be ample, but not roomy. It was decided that the patient was not in labor. She was given 3 gr. of nembutal and asked to remain in the hospital. The entire next day and night she had only slight abdominal pains. On the morning of March 18 the patient was still not in labor. The roentgenologic opinion was that the baby was normal in size, in R.O.P. position, the head was above the inlet, and that apparently there was no disproportion between the size of the pelvis and the size of the baby. Accordingly, it was decided that the patient was entitled to a real trial labor before any operative intervention was contemplated. She was discharged from the hospital and told to return at the onset of strong, regularly recurring, abdominal pains. She began to suffer such pains at about 9 P.M. that same day (March 18) and called at midnight to say that "her waters had broken." At 3 A.M., March 19 she entered the hospital, having rather strong uterine contractions recurring at five-minute intervals. Aside from the usual preparation and a hot soapsuds enema, she received no other medication.

At 7:30 A.M. she was having such strong contractions, lasting thirty to forty seconds, and recurring at two- to three-minute intervals, that she was decidedly uncomfortable, and 1/6 gr. of morphine sulfate was administered. This afforded her little relief. At 8 A.M. an abdominal examination revealed an unengaged head in R.O.P. position. It was decided that she had had an adequate trial labor, and therefore a low flap cesarean section was done at 8:30 A.M. March 19, under cyclopropane anesthesia. The blood loss was minimal, operating time 45 minutes. She was delivered of a normal male child, weighing 8 pounds 11 ounces, which cried spontaneously.

Her postoperative convalescence for the first five and one-half days was unusually smooth, the patient voiding spontaneously, complaining only of occasional gas pains, and having only three single elevations of temperature on three successive days, the highest of which was 100.6° F. and the lowest 100.2° F.

She was feeling especially well on March 24, beginning her fifth postoperative day, until 6:30 P.M. when she had a severe chill with a temperature of 103.6° F. Her only complaint was a short, dry, hacking cough. Examination at 8:30 P.M. revealed an acutely ill patient, having a temperature of 103.6° F., pulse 140, respiration 40. Breathing was labored, but not painful. The chest was free of signs except for a small area of dullness and diminished breath sounds at the right base. The abdomen was quite soft, not distended, and not tender to palpation. The wound was clean and dry, healing by primary intention, and showed no signs of tenderness or induration. Pelvic examination was deferred to the next morning when a cervical culture was to be taken. A catheterized specimen of urine at this time was negative except for a faint trace of albumin. A presumptive diagnosis of an embolic pneumonia arising from a pelvic thrombophlebitis was made.

It was because of this, i.e., that the pneumonia was thought not to be an inhalation pneumonia, and therefore probably not due to the pneumococcus, that the patient was placed on 20 gr. of sulfanilamide every four hours with 5 gr. of sodium bicarbonate, instead of sulfapyridine.

The next morning, March 25, the patient was worse, acutely toxic, markedly cyanotic, presumably as a result of the sulfanilamide, temperature ranging from 104.5° to 105.5° F. Aerobic and anaerobic plates were taken from the cervix, and aerobic and anaerobic blood plates were taken. A complete blood count, blood typing, throat culture (in view of the fact that no sputum was available), and portable x-ray of the chest were ordered. Pelvic examination at this time was noninformative. The uterus was involuting well, not tender. The parametria were clear, the lochia was normal in amount and color, and was not particularly foul. The x-ray of the chest showed a small, irregular patch of incomplete consolidation in the inner portion of the right lower lobe adjacent to the right border of the heart. The red cell count was 5,040,000 and 10½ Gm. Hb.; white count was 28,800, and 95 per cent polymorphonuclears.

Although she had received 160 gr. of sulfanilamide by the morning of March 26, the patient grew steadily worse. It was this morning that the blood culture taken the previous day showed a growth of approximately 1,200 colonies of *Staphylococcus*

aureus per cubic centimeter. The uterine culture also showed a preponderance of *Staphylococcus aureus*, about 75 per cent, along with *B. coli*. Both anaerobic plates also showed *Staphylococcus aureus*, but no anaerobic organisms. The throat culture showed the usual bacteriologic flora, having some pneumococci and short chain streptococcic. The sulfanilamide was then discontinued, and sulfamethyl thiazol therapy was started.

At 1:45 P.M. of March 26, 2 Gm. of sulfamethyl thiazol were given by mouth and 1 Gm. every four hours from then on was ordered. Five grains of sodium bicarbonate were given with each dose of sulfamethyl thiazol. For the first few days, the patient complained of epigastric pain soon after taking the medication, which was quite severe, occasionally requiring codeine phosphate by hypodermic injection for relief. The pain, however, was of short duration and after a while it never recurred. There was no nausea nor vomiting, and the cyanosis was definitely less than that from sulfanilamide.

On the next day, March 27, although the temperature levels were a little lower, the patient complained of a painful right shoulder joint which was exquisitely tender on palpation, although not red nor swollen. It was felt that she was developing a septic arthritis, and this was more or less substantiated by the fact that coincident with the development of the painful shoulder joint there appeared about six small furuncles on the skin of her back and right buttock. Unfortunately, no cultures were taken from these although one on the buttock had to be incised.

Another blood culture and complete blood count were done on this day. The blood count showed a red cell count of 4,480,000 and 9.9 Gm. Hb.; white blood count, 23,400 and 95 per cent polymorphonuclears. She was given 250 c.c. of citrated blood. The blood culture the next day was reported as showing a growth of 240 colonies of *Staphylococcus aureus* per c.c. of blood. The dose of sulfamethyl thiazol was increased to 1½ Gm. every four hours. She was definitely improved on March 28. She was more comfortable, her temperature levels were lower, and she only had occasional spells of drenching perspiration which previously had recurred with annoying frequency.

Another blood culture and complete blood count were done on March 29. The blood count showed 3,660,000 red blood cells and 8.5 Hb.; white blood count 21,250 and 89 per cent polymorphonuclears. There was no growth in the blood culture in twenty-four hours, but in forty-eight hours there was a growth of 2 colonies per c.c. of blood. She was given a transfusion of 250 c.c. citrated blood on March 30.

A catheterized specimen of urine on March 30 was negative. Her improvement was marked by April 1. An x-ray of the chest taken then showed evidence of possible beginning resolution from a larger pulmonic field in the right lung than had been originally involved. The left lung was negative. A blood culture taken this morning (April 1) proved to be sterile. Her blood count was 3,260,000 red blood cells and 9.7 Gm. Hb.; white blood cells 18,800, and 85 per cent polymorphonuclears. The dosage of sulfamethyl thiazol was decreased to 1 Gm. every four hours. On April 2 and 3, the highest temperature level was 100.8° F. On the morning of the fourth the dosage of sulfamethyl thiazol was decreased to 1 Gm. every day. She had received 66 Gm. or 990 gr. up to this day. On the night of the fourth her cough was becoming more pronounced and her evening temperature rose to 102° F. This repeated itself on the fifth, so the dosage of sulfamethyl thiazol was increased to 1 Gm. every six hours. A blood count was done on April 6 and showed 3,400,000 red blood cells and 9.5 Gm. Hb.; 18,400 white blood cells and 77 per cent polymorphonuclears. The patient was feeling quite well, appetite excellent. Her only complaint was an annoying cough which was controlled with codeine, and an evening elevation of temperature to 102° F.

On April 1, on inspection of her wound, there was a small, superficial separation near the inferior angle from which a scant serosanguineous discharge could be expressed. On April 6 this discharge had become more profuse and definitely purulent. The opening was widened with a hemostat and a rubber dam drain inserted. A culture from the wound showed *Staphylococcus aureus*. However, there was no tenderness nor induration, and it was felt that the wound could not account for her fever. On the afternoon of April 7 the patient complained of drowsiness

for the first time. There was a peculiar discoloration of her skin resembling jaundice. There was an ecchymotic area about 3 inches long and 1 inch wide over the external malleolus of her right ankle which was tender to touch. Her temperature was 101.8° F. Her chest was negative on examination, although she still had a cough. Pelvic examination again revealed a perfectly normal, nontender, firm, mobile, involuting uterus with no parametrial involvement. Sulfamethyl thiazol therapy was ordered cut, as it was thought that the patient was suffering from drug intoxication. Up to this time she had received a dosage of 10⅔ Gm. of sulfanilamide and 78 Gm. of sulfamethyl thiazol, making a total of 88⅔ Gm. or 1,330 gr. An x-ray of the chest the next morning showed no further extension of the pneumonic process. Her temperature had risen to 103.4° F., and there was insufficient involvement in either the chest or the pelvis to account for this. Her blood culture was sterile. A catheterized urine specimen was negative for pus, bile, or urobilinogen. The direct van den Bergh's test on her blood was negative. The discoloration of her skin was then thought to be due to the azo dye of the drug. Her blood count showed a definite leucopenia, having a total white count of 6,800 with 78 per cent polymorphonuclears. Forty-eight hours previous to this her count had been 18,400 with 77 per cent polymorphonuclears. There was no depression of her red cells or hemoglobin. She was given a transfusion of 500 c.c. of citrated blood. The next day, April 9, the white count was 6,000 with 61 per cent polymorphonuclears. However, despite this further depression of white cells, the patient was remarkably improved. Her temperature had dropped to normal. Her drowsiness had completely disappeared. The color of her skin was normal, and the ecchymotic area on the right ankle had faded. In her own words, "she felt like a new woman and had not a complaint in the world." With her temperature absolutely normal on the tenth and eleventh of April and with no complaints, a false sense of security was felt, so that no blood counts were done on those days. On April 12 the possibility of allowing the patient to dangle her legs was being considered when that afternoon she developed a temperature of 103.4° F. She appeared quite toxic. Complete physical examination was negative. That morning the wound had been dressed, found to be dry, with no discharge. The rubber dam which had been reinserted daily was now removed and left out. The wound was reinspected in the afternoon, probed, but absolutely no discharge was forthcoming. Complete blood count showed 3.39 million red blood cells with 10.5 Gm. Hb.; a white cell count of 1,750 with 4 per cent polymorphonuclears, and 9 per cent mononuclear cells. Her throat was absolutely negative. There was no evidence of angina now nor at any subsequent time. She was given 300 c.c. of citrated blood the next morning with 3 c.c. of liver concentrate (45 units U.S.P.) intramuscularly. Prior to this, a count done revealed 2,350 white blood cells with no polymorphonuclears. The only granular cells present were 2 per cent basophiles. She had 16 per cent mononuclear cells. The reason the percentage of mononuclears is mentioned is because some authors feel that the occurrence of a monocytosis in a granulocytopenia is a good prognostic sign. She was acutely ill for the two succeeding days, her temperature ranging from 101° to 104° F. She was given a transfusion on both of those days, receiving 500 c.c. citrated blood on the fourteenth and 300 c.c. on the fifteenth, and 3 c.c. of liver concentrate parenterally. By the morning of April 16 the patient was quite well again, her temperature being practically normal all day. Her blood count, which had been mounting steadily, had now reached 7,100 with 49 per cent polymorphonuclears. The majority of the polymorphonuclears were juvenile forms and their cytoplasm contained large, deep-staining, coarse granules which had been termed "toxic granules" but are only indicative of immaturity. The monocytosis continued increasing, reaching 19 per cent on the sixteenth of April. Strangely enough, with the blood count approaching normal, the wound began to drain pus again. Unfortunately, her blood count did not remain normal, but continued to rise so that she developed a leucocytosis. Her white count reached 19,350 with 74 per cent polymorphonuclears on April 20, and 20,700 with 85 per cent polymorphonuclears on April 29. As her white count rose, the percentage of young polymorphonuclears dropped to normal levels, and the so-called "toxic granules" disappeared. The percentage of mononuclears coincidentally dropped to normal levels. The patient felt quite well but continued to run

a low-grade temperature on certain days. The temperature and leucocytosis were cause for concern so far as there was nothing in the physical examination to account for them. The wound was practically healed and had only a scant purulent drainage. When her temperature reached 101.8° F. on May 1, the apprehension felt was sufficient to repeat a blood culture which proved to be sterile. It was only after the report of this culture was back that it was decided that her fever and leucocytosis were merely manifestations of bone marrow hyperactivity. So, throwing caution to the winds, she was allowed out of bed. Her temperature then found normal levels and remained so to the day of her discharge. Her white count, however, was 17,300 with 75 per cent polymorphonuclears on May 6, the day before her discharge. After fifty-three days in the hospital she was discharged on May 7 with her baby, who now weighed 10 pounds 3 ounces.

COMMENT

Sulfanilamide in the past has been most disappointing in the treatment of staphylococcus infections. The remarkable and dramatic response of this patient's sepsis to sulfanilamide's derivative, sulfamethyl thiazol, leaves little room for the argument of coincidence.

Agranulocytosis is probably the most serious complication that might follow the administration of sulfanilamide or its derivatives, so far as the large percentage of the cases (53 per cent in a study of the 30 cases reported[1-26]) developing this type of blood dyscrasia eventuate in death. The incidence of agranulocytosis with this form of chemotherapy is not particularly great and fortunately occurs only after prolonged administration of the drug. The smallest dose thus far reported as having given rise to agranulocytosis in an adult is 18 Gm.[24] and that patient recovered rather promptly. The average dose responsible for agranulocytosis in an adult was 57.7 Gm.[1-26] Despite the infrequency of agranulocytosis as a complication, the gravity of its occurrence makes close vigil a sine qua non of prolonged administration of the drug. The late appearance of malaise, drowsiness, and unexplained fever calls for immediate withdrawal of the drug, even though the blood count may give no indication of an impending granulocytopenia. The precipitate suddenness with which granulocytopenia may occur is manifest in the case reported above.

The impression obtained from a study of 30 cases[1-26] (including the author's case) of agranulocytosis following sulfanilamide therapy is that the prognosis depends not upon the treatment given but upon the severity of bone marrow depression that has occurred and the time of the withdrawal of the drug, i.e., a case has a much more serious prognosis if the drug has been administered up to the occurrence of agranulocytosis than if the agranulocytosis has occurred several days after the withdrawal of the drug.[1, 14, 17, 24]

It is interesting to note that 16 per cent of those cases[1, 14,17, 24] had a monocytosis during the granulocytopenia and all of them recovered.

A study of the hematologic charts in the 30 cases referred to above showed that four (besides the author's) had a leucocytosis following the agranulocytosis but none of the authors commented upon the unusual nature of this occurrence, nor did they state whether there was anything present to explain the increased white count. However, in a very commendable article on agranulocytosis, Damashek reported the occurrence of a leucocytosis after granulocytopenia had first been artificially induced with amidopyrine and then withdrawn. He refers to it as a "release phenomenon." If a toxic depression of bone marrow can give rise to an acute illness with high temperatures, it does not seem unreasonable to assume that a hyperactive bone marrow in its regenerative phase can also produce some temperature and leucocytosis.

I should like to express my thanks to Winthrop Chemical Corporation for their kind cooperation, and to Mr. Joseph M. Chernaik for his invaluable assistance in doing the laboratory work.

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MATERNAL DEATH CAUSED BY HEMORRHAGE IN THE ADRENALS*

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SUPRARENAL hemorrhage in the adult is an unusual condition almost invariably associated with other pathology in the body. Extensive hemorrhage with parenchymal destruction and suprarenal failure has been found co-existing with and furnishing the immediate cause of death in a number of widely diverse conditions. Among these reported in the literature are cases of epilepsy, extensive neoplasm of right lung compressing the vena cava, metastatic carcinoma of the adrenals and other intraabdominal organs, agranulocytic angina, bacterial endocarditis, staphylococcus pyemia, meningococcic bacteriemia, and one of advanced diffuse arteriosclerosis with subacute nephritis. In the following case report, suprarenal hemorrhage and necrosis were co-existent with unilateral hydronephrosis and bilateral pyelonephritis. There has been no previous report, I believe, of this condition as a causative factor in maternal death.

Mrs. M. P. (Hospital No. 28556), a 35-year-old white multipara, was admitted to the Fitkin Memorial Hospital on June 23, 1939. She was the wife of a poor tenant farmer living in an isolated portion of Monmouth County; this woman had received and apparently needed no medical attention during the pregnancy which had advanced to the thirty-sixth week at the time of her acute illness and premature labor. Three children had previously been born to her at home, apparently without complications. The ages of the children are 14, 9, and 4. The physician who attended the confinement in all three cases knows of no disability or illness suffered by this patient. She worked hard continually.

The severely painful seizure which initiated the present illness began at 5 A.M. on June 23. The doctor who was called reached the patient's home at 7 A.M. and found her in extreme pain. The entire upper abdomen was rigid with great tenderness and pain in the right costovertebral region. There was no vomiting. The woman's pregnant condition was obvious, but it was questionable whether she was in labor or not. Hospitalization was advised because of the woman's acute illness and poor general condition. Blood pressure was not taken at home but the attending doctor thought the degree of shock was considerable. No morphine or other opiate was given.

Transportation to the hospital by ambulance was not effected until 12 noon. A marked state of shock was apparent at time of admission. The woman was conscious and cooperative. The pulse was rapid and almost imperceptible in the radial vessels. The respirations were labored. Blood pressure was 50/??, and

*Read at a meeting of the New York Obstetrical Society, May 14, 1940.

rectal temperature 102.4° F. Severe abdominal pain was the chief complaint, the abdominal muscles were rigid, and uterine contractions were not definitely felt at first. After ¼ gr. of morphine and an intravenous infusion of 500 c.c. of 10 per cent dextrose had been given, the blood pressure was 70/30. Pulse was 132. Intermittent uterine contractions could then be felt. No fetal heart sounds were heard at any time. At 1:30 P.M. vaginal examination showed the cervix to be completely effaced and three fingers dilated. The membranes were ruptured artificially and amniotic fluid heavily stained with meconium escaped. Breech presentation was diagnosed. Within two hours spontaneous expulsion of a stillborn male fetus, weighing 2,870 gm., was accomplished, followed quickly by complete placental separation without unusual bleeding. One ampoule of ergotrate was given intravenously.

Subsequent to delivery the patient fell asleep and profuse diaphoresis was noted. The pulse became stronger, rate 120. Blood pressure was 80/40. The temperature at 4 P.M. was 98.8° F. and at 8 P.M. 98.2° F. Throughout the evening and night the condition remained much the same. The patient slept intermittently, was thirsty

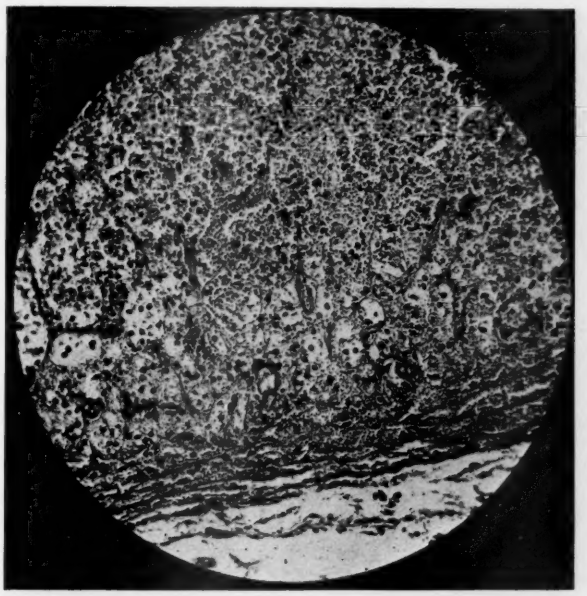


Fig. 1.—Section of adrenal showing hemorrhage. ×350 diameters.

when awake, and took fluids well. Micturition was spontaneous. Blood pressure remained low, systolic 60 to 70. Color was poor. Intravenous infusions of 10 per cent dextrose were given in the evening and in the early morning, the latter after threatened collapse was evidenced by cold clammy skin, weakening pulse, and blood pressure of 40/?. At breakfast time the patient had rallied somewhat and enjoyed cereal. She also ate what was offered for luncheon and remarked that she felt fairly well.

Throughout the day, however, the extremities were cold and cyanotic, the pulse rapid and almost imperceptible, and the systolic blood pressure was persistently under 70. The abdomen was soft and not distended, the uterus firmly contracted, and lochia moderate.

About 6 P.M. sharp pain in right chest was mentioned and at 6:30 P.M. a "shaking" chill occurred. The breathing which had been labored all day became more difficult. Coarse moist râles were heard in both lung bases. In the evening cyanosis deepened and circulatory failure increased. Use of oxygen tent gave no relief. The patient died at 11:00 P.M. (thirty-two hours after delivery).

Urinalysis (catheterized specimen) June 24, showed specific gravity, 1.013; albumin, heavy cloud; and hyaline and granular casts; red blood cells and clumps of leucocytes were found in the sediment.

Blood count June 24, red blood count, 3,840,000; hemoglobin, 73 per cent; white blood count, 22,100, and polymorphonuclears, 87.

The autopsy showed 80 to 100 c.c. of fluid in each pleural cavity, with pneumonia of right lower lobe, congestion of left lung base, and pericardial effusion. Within the abdomen a fairly large amount of blood-tinged fluid was found, along with petechial hemorrhages into the mesentery and edema of the parenchymatous organs. On section the liver showed cloudy swelling and diffuse hemorrhage. Both kidneys were enlarged, the right more than the left. There was hydronephrosis on the right side and the kidney pelvis contained gravel and two stones. As the ureter entered the bladder three stones were impacted. Microscopic study of both kidneys showed pyelonephritis.

The adrenal glands were slightly swollen. Both showed pericapsular hemorrhages and on section there was also subcapsular hemorrhage infiltrating through the cortex into the medulla. Microscopic study showed normal structure nearly obliterated. In the best preserved portions the reticular and vesicular layers can still be made out in places but even here extensive hemorrhage is present. Low and high magnifications of the other places in the adrenal show extensive necrosis and hemorrhage without any characteristic adrenal cells. There was no blood vessel thrombosis.

CONCLUSION

Based upon clinical course and post-mortem examination findings it seems indisputable that the adrenal hemorrhage and necrosis was the cause of death in this case. (Toxemia dependent upon pyelonephritis seems the most reasonable predisposing factor in causation of this rare adrenal damage.) The nature of the acute seizure forty-two hours before death may be debated. Although the right ureter was obstructed by calculi impacted near the bladder orifice it seems unlikely that renal colic produced the initial pain. I believe that labor and delivery made little or no contribution to the state of shock, and pregnancy had nothing to do with any of the outcome. Adrenal damage is the probable explanation for the initial pain, abdominal rigidity, pyrexia, and shock. Adrenal insufficiency persisted and led to the fatal outcome, the terminal pneumonia being incidental.

DISCUSSION

DR. HERBERT F. TRAUT.—These microscopic preparations remind me very much of the pictures that have been published by Georgy and his co-workers of experimental animals which were given a diet deficient in choline. These animals showed not only the fatty type of degeneration of the liver, but also massive hemorrhage of the adrenals, involving, first, the medulla, and much later, the cortex of the adrenal.

I suggest this as the possible etiology. It is possible that the patient's diet was not adequate and that avitaminosis may have figured in the etiology of this case.

DR. SAMUEL H. GEIST.—As Dr. MacKenzie has stated the clinical diagnosis of adrenal insufficiency is extremely difficult. If, however, we are fortunate enough to make such a diagnosis or even suspect it, it might be worth while to try the effect of desoxycorticosteron, which might temporarily tide the woman over her primary shock and enable her to offer some resistance to an infection which might follow labor. What this therapy might offer I do not know but it is worth trying. Short of this we are absolutely helpless in the face of such a critical condition.

DR. N. M. ALTER.—While it may not be germane to the topic under consideration, I would, first, like to call attention to an article by Dr. Robert Frank in which he speaks of the adrenal being the master gland, probably taking the place of the pituitary gland, and that it has not been given the attention it deserves.

This case demonstrates that the probable indirect cause of death was the septicemia, but the direct cause was shock brought about by massive hemorrhage

into the adrenal. This has been known in obstetric practice, especially in infants and particularly in connection with marasmus, where we find it more extensive than it was in this particular case. In adults, the most common variety was that described in this country by George Cahill, in the adenomatous type of tumors, either malignant or benign. I had a case at the Margaret Hague Maternity Hospital where the woman died suddenly of unexplainable shock after parturition, due to an adenoma with no massive hemorrhage. In the case reported by Dr. MacKenzie the massive hemorrhage occurred in a practically normal adrenal without tumor formation, which, from a survey of the literature, is rather unique. I studied the sections submitted to me and the different portions showed barely recognizable adrenal structure; most of it was completely destroyed by hemorrhage and necrosis. The necrosis was due to vascular change, so there must have been some circulatory damage, but one cannot say whether it was due to septicemia.

I think that in this unusual case we should focus attention on the adrenal with the occurrence of sudden shock in a very acute, almost surgical, condition. In this patient the adrenal was practically normal before the lesion presented developed.

CHORIOEPITHELIOMA

Associated With Tubal Pregnancy and Pulmonary Metastases. High Gonadotropin and Low Pregnanediol Values.

Joseph T. Smith, M.D., and Nicholas T. Werthessen, Ph.D.,
Boston, Mass.

(From the Joseph H. Pratt Diagnostic Hospital)

CHORIOEPITHELIOMA has been studied so extensively and so many cases of the condition have been reported, that only some features of special interest connected with the one we are presenting induce us to offer this summary.

This 37-year-old housewife was admitted to the Joseph H. Pratt Diagnostic Hospital, Oct. 18, 1939. She complained merely of "Not feeling good." For three or four weeks, she had been regurgitating a spoonful or so of whitish, sour, yellowish fluid upon arising in the mornings. There was a history of old gonorrheal infection. The family doctor had the patient admitted for study to decide whether the symptoms were due to pelvic inflammatory disease or to possible cholecystitis.

In January, 1939, she had had a ruptured tubal pregnancy (left). At operation, the tube and ovary were removed from that side, with excision of the uterine cornu. The right tube was tied. The patient made a fairly good recovery, complicated only by an attack of left-sided pleurisy. There was one almost normal period in March, 1939. There were none after that up to the date of admission to the Pratt Hospital.

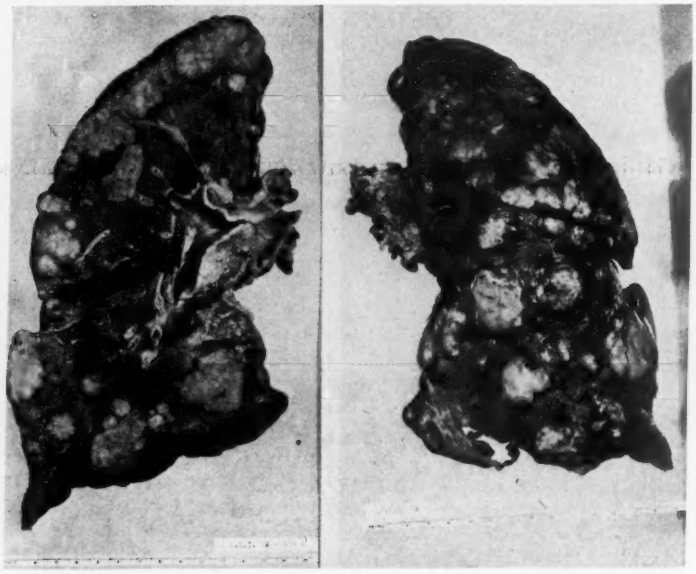
She had been married eleven years, and had had two children, aged 10 and 7½ years. There was one induced abortion at two months about six years before admission. The only other pregnancy was the tubal one in January, 1939. On admission her weight was 135 pounds, a drop of 15 pounds from normal in a period of about six weeks. The blood pressure was 110/70. The urine showed a slight trace of albumin; no casts. There was mild secondary anemia; red blood cells, 3,510,000; and hemoglobin, 62 per cent. The blood sedimentation rate was always at a high figure, from 80 mm. to 90 mm. in one hour. The leucocytes were 7,300.

On careful physical examination, astonishingly few abnormal findings were discovered. The lungs seemed clear and resonant throughout; no râles were heard. The breath sounds were of good character; there was no adventitious rub at any point. This fact was demonstrated with special care on the left side, where there had been a pleurisy in January, 1939.

In the pelvic region, a rather hard nodular mass was felt just to the left of the midline above the pubis.

Vaginal examination showed marked thickening and cauliflower-like configuration around the urinary meatus. A granulation-like area at the side of the urethra presented a red papule that had been bleeding. The uterus was continuous with a firm mass which filled the left side of the pelvis and extended about 6 cm. above the pubic bone. A second vaginal examination, four days later, showed a hard nodule halfway up the posterior vaginal wall, about 3 mm. in diameter. It was not believed that this nodule had been present at the time of the first examination.

On Oct. 24, 1939, a Friedman pregnancy test gave a strongly positive reaction. The same day, a biopsy specimen was removed from the mass at the urethral meatus. The microscopic report showed "an invading chorioepithelioma. The tumor is composed of sheetlike masses of mononucleated tumor cells interspersed with many large multinucleated giant tumor cells. There is no stroma except around small blood vessels. The tumor is rapidly growing, is destructive in its invasive course in the normal tissue included in the sections. There is erosion and invasion of blood vessels and small hemorrhages; and there are numerous varying-sized areas of necrosis of tumor cells."



A. *B.*

Fig. 1.—Metastatic tumor. *A*, Sagittal section of right lung. *B*, Posterior surface of right lung.

At the same time, an x-ray plate of the chest showed: "The lung fields present innumerable dense round areas of infiltration of different sizes. . . . The findings are those of malignant metastases. From the history and clinical findings, chorioepithelioma is the most likely origin of these metastases."

This patient, while in the Pratt Hospital, showed a remittent fever throughout three weeks. The temperature never went over 100° (F.). A total of twelve x-ray treatments were given to the front and back of the chest. In spite of these, both clinically and by x-ray examination of the chest, the tumor grew rapidly. The patient returned home. Later, there was urinary obstruction, uremia developed, and death occurred Feb. 2, 1940.

At autopsy, permission was not given to open the head.

Many findings were simply terminal in origin, and need not be listed here. The interesting ones, apart from the old pelvic adhesions, were a chorioepithelioma of the uterus, with metastases in the vagina, lungs, right kidney, and small intestines. The uterus measured 15 by 9 cm. The upper half, to the left, consisted of a round

shaped, well-defined and demarcated, grayish brown, mushy mass which extended to the serosa without penetrating it. Here, the surface was of a reticulated or irregularly granular appearance. Microscopic examination of this tumor mass, and of all the metastatic masses, showed the same picture observed in the original slide from the biopsy specimen.

Here, then, we have a case of chorioepithelioma that certainly must have developed from the tubal pregnancy removed nine months before the tumor was diagnosed. We get so used to associating chorioepithelioma with hydatidiform mole that we may overlook the fact that fully half of the cases of chorioepithelioma do not follow moles. Here, we have one starting in a tubal pregnancy. If we overlook the possibility of tumor even when there has been no mole, we may lose vital time in making a diagnosis. This tumor, starting in the tubal stump, did not have any thick myometrium to penetrate. It was practically in the peritoneal cavity from the beginning, so its dissemination was rapid. Another point of interest was the fact that lungs so involved with tumor masses should give so few symptoms and signs. The x-ray was taken more or less as a matter of routine, because the patient told of a little cough that had hung on for some weeks. Yet this cough had been so slight that it had not been mentioned until the patient was directly questioned. Even after the x-ray plate, showing massive tumor growths, had been examined, physical percussion and auscultation of the lungs showed astonishingly

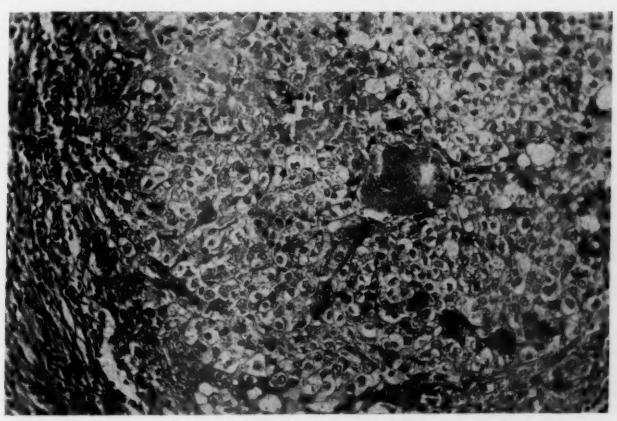


Fig. 2.—Vaginal wall metastasis. Sheets of syncytial cells, giant cells, invasion of vein.

little abnormal change. Yet, at autopsy, it was estimated that at least 50 per cent of the cubic volume of the lungs consisted of tumor tissue. Vaginal bleeding, usually a striking feature in cases of chorioepithelioma, did not appear with this patient. Probably this was due to the fact that the tumor originated near the peritoneal surface of the uterus instead of arising within the uterine cavity, as it more usually does.

Assays of endocrine hormones showed some interesting results. Dr. Werthessen will report more complete findings elsewhere. However, the striking finding from this assay is the enormous quantity of gonadotropic hormone, the luteinizing factor, which was present.

By the method of assay, much of this estrone may be in the form of estradiol.

Any attempt to offer "normal" figures is really inaccurate and unfair. The averages in Table I are presented merely for comparison.

We might expect to find such large amounts of chorionic gonadotropin (B). A more surprising reading is the low pregnanediol. A persisting corpus luteum is almost the rule with hydatidiform mole and with chorioepithelioma. That strong luteinizing influence would lead one to expect a great activity of the lutein cells, with a corresponding high value for the pregnanediol. This condition, however, was not found. In this connection, it may be mentioned that at autopsy only the right

TABLE I

	PATIENT	NONPREGNANT, NORMAL	PREGNANT, NORMAL
Chorionic gonadotropin, "B"	1000 R.U. *plus* per 100 c.c. serum	Trace	100-500 R.U. per 100 c.c. serum
Estrone	1,000 gamma per 24 hours*	50 gamma (lower limit)	100 gamma
Estriol	100 gamma per 24 hours*	Twice the Estrone	500 gamma
Pregnanediol	3.6 mg. per 24 hours	4-8 mg. per 24 hours	8 mg. per 24 hours at eighth week, increasing to 75 mg. late in pregnancy

*Ratio, estrone to estriol, is almost the reverse of normal.

ovary was seen, as the left had been removed at operation. This remaining right ovary was said to have an atrophic appearance, and no corpus luteum was present.

SUMMARY

A case of chorioepithelioma is presented which followed a left tubal pregnancy, showing almost none of the usual signs and symptoms, and spreading by metastasis to the lungs before it was recognized locally. Hormone assays showed high chorionic gonadotropin and low pregnanediol values.

30 BENNET STREET

PRIMARY OVARIAN PREGNANCY

SOPHIE NOWAKOVSKY, M.D., CHICAGO, ILL.
(From the Women and Children's Hospital)

BECAUSE of the rarity of ovarian pregnancy, particularly of proved cases, the following striking example is reported:

L. S., a white, married housewife, 32 years old, was admitted to the Women's and Children's Hospital on April 15, 1939, to the service of Dr. Giryotas, to whom I am indebted for permission to report this case. The patient complained of pain in both lower quadrants of the abdomen of three weeks' duration.

She began to menstruate at 12 years of age. Periods occurred every twenty-six to twenty-eight days and lasted six to seven days, with heavy flow and slight cramps.

She was married at 24 years of age and had 3 pregnancies. The oldest child was 7 years of age; the youngest 7 months. Lacerations complicated the first pregnancy; forceps were used in the last pregnancy. There was no history of miscarriage or abortion.

The patient had been in good health until Feb. 19, 1939. Following the last pregnancy, her periods were resumed. On Feb. 19, 1939, the patient thought that she was beginning to menstruate; however, this period, instead of ending in a week, continued for over thirty days. At first, bleeding was very profuse. Later it ceased for two or three days and then recurred. Clots were present only on one day.

On March 24, 1939, one day after bleeding stopped, the patient complained of a sharp, shooting pain in both lower quadrants which was so severe that it caused her to remain flexed and quiet. Neither hypodermic injection of morphine nor application of electric pad relieved the pain. There was some relief from use of

an ice bag. The pain never fully subsided. It was accompanied by dysuria but not by nausea or vomiting. Before entry to the hospital the pain radiated to the epigastrium.

Physical Examination.—Temperature was 98.4° F.; pulse, 70; respiration, 20.

The patient was a thin white woman, apparently in no great distress. Pupils reacted to light and accommodation. Breasts were atrophic; nipples inverted. Lungs were clear and resonant. The heart rate was regular. Abdominal rigidity and spasm were not elicited. There was marked tenderness above symphysis, more on the right side. The introitus admitted two fingers. Both adnexa were markedly tender. On vaginal examination no masses were felt except for what appeared to be a retroverted uterus. But on rectal examination the "retroverted uterus" was thought to be a distinct mass posterior to and connected with the uterus. The first clinical impression was ruptured ectopic pregnancy.

Operation (Apr. 17, 1939).—The peritoneal cavity contained bloody fluid. Left oophorectomy, bilateral salpingectomy, and appendectomy were carried out. The postoperative course was uneventful. Patient was discharged April 29, 1939.

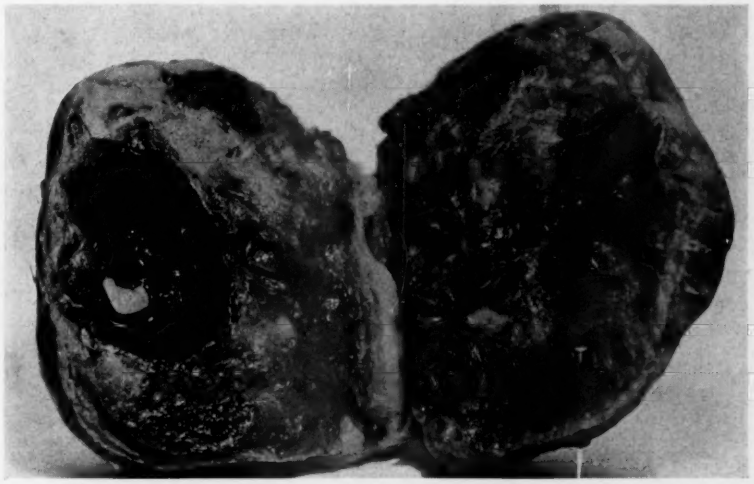


Fig. 1.—Cut surface of ovary. Note the amniotic sac with the embryo on the left side.

Macroscopic Description of Specimens.—The left ovary measured 7 by 5 by 4 cm. The surface was nodular and showed no evidence of adhesions. A gross rupture through the surface was not seen. The nodules were only slightly elevated. Shining through the capsule were varied colors, ranging from brown to gray. The consistency of the mass was firm except in the midsuperior portion where it was cystic. On section the cystic area revealed itself as a sac which measured 3 by 2.5 cm. on the cut surface. The lining was a thin, blue, glistening, smooth membrane which was irregularly elevated by the underlying wall. The content of the sac consisted of a slight amount of blood-tinged, thin fluid. In addition, the sac contained a small blood clot. Floating in the fluid content was a well-formed embryo about 0.9 cm. in length. The embryo lay in the posterior half of the sac, attached to the inferior wall by a bluish umbilical cord about 1.2 cm. long and less than 1 mm. thick (Fig. 1).

The sac was situated in the ovarian mass 0.5 cm. from the superior surface, 1.2 cm. from the medial, 1.8 from the lateral, and 3 cm. from the inferior surface. The tissue surrounding the sac showed extensive hemorrhages of yellow brown color. In the inferior-medial border of the mass preserved ovarian structure could be discerned, measuring 3 by 1 cm. The attached tube was 5.5 cm. long and 0.5 cm. thick. Its surface was smooth and glistening. The fimbriated end was patent and normal in appearance. The lumen was not distended. It contained no blood. The wall was

not thickened. The right tube was 6 cm. in length, and revealed no remarkable changes. The appendix was 6.2 cm. in length; the serosa was injected.

Microscopic Findings.—Ovary: Sections taken from the ovary revealed typical findings of primary ovarian pregnancy. The chorionic villi showed varying stages of regressive changes (Fig. 2). There was diffuse recent hemorrhage; necrosis of the ovarian stroma and leucocytic infiltration in the surrounding tissue. Occasional trophoblasts were seen in the vicinity of the blood vessels. In sections examined, no lutein tissue was made out. In certain sections, preserved ovarian stroma formed the external surface. No sections were made through the embryo, as it was desirable to save the specimen intact.

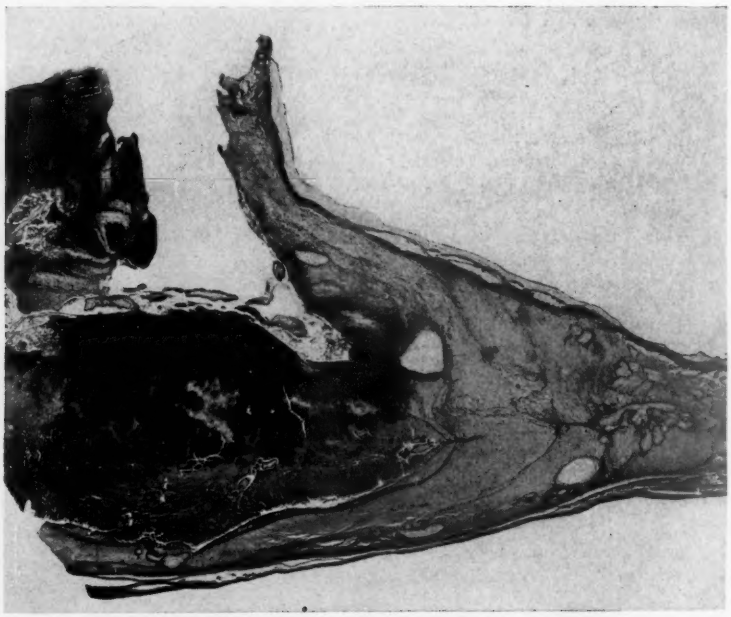


Fig. 2.—Low power of a section through the ovary. Note the outer shell of ovarian stroma, the hemorrhage, and the chorionic villi throughout the section.

Tube: The lumen was free. Tunica propria in some fimbria was slightly thickened. Outer layers showed marked edema with injection of vessels. There was moderate, more focal perivascular infiltration of round cells and plasma cells. A thin layer of fibrin intermixed with red blood cells was present on the serosa. In one site where mesothelium was hyperplastic, there were deposited brown granules, apparently hemosiderin.

Appendix: Foci of lymphocytes and plasma cells were noted around the blood vessels of the serosa and subserosa, presenting a picture of a so-called disproportion periappendicitis due usually to involvement of an adjacent organ.

UNIVERSAL EDEMA OF THE FETUS IN EACH OF MONOCHORIONIC TWINS WITH PATHOLOGIC FINDINGS (ERYTHROBLASTOSIS FETALIS)

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LABOR was normal. Twin A was delivered by breech extraction and Twin B by podalic version and breech extraction. Both deliveries were moderately difficult. The babies were females, Twin A weighing 2,891 Gm. and Twin B 3,350 Gm. They were quite similar in appearance, both presenting generalized mild icterus and marked pitting edema of all subcutaneous tissues, particularly over the scalp, neck, and posterior thorax. The abdomen of each baby was greatly distended. In each the liver and spleen could be palpated 6 cm. below the costal margins. The fetal heart beat for five minutes in each baby, but respirations were never established.

The placenta was about twice normal size and very edematous. There were two cords, two amniotic sacs, and one chorion. The circulation of the placenta was that of monovular rather than biovular twins. Both babies died before blood studies could be made.

*Gross Pathology.**—On opening the body of Baby B, a large amount of bile-stained fluid ran from the cut surfaces. The thoracic organs were all present and in normal relationship. Each hemithorax contained 10 c.c. of bile-stained pleural fluid. Lungs were atelectatic, but otherwise heart and lungs were normal.

There were approximately 100 c.c. of bile-stained fluid in the peritoneal cavity. There were no abnormalities of the organs, including the thoracic duct and bile ducts. The liver and spleen were grossly enlarged and firm.

The brain was very friable, but otherwise normal.

TABLE I. TABLE OF COMPARATIVE WEIGHTS

	NORMAL	BABY B	BABY A
Heart	21	36	35
Liver	134	200	145
Spleen	10	27	15
Kidneys (combined)	23	30	24
Brain	363	300	300

The placenta was unusually large and edematous. Two cords were attached. The maternal surface was boggy, variegated gray, yellow and red with the cotyledons prominent. Wharton's jelly was increased and was edematous.

Microscopic Pathology—Review of Sections (Baby B).—

Skin: The stratum corneum presented a loose alveolar structure due to the marked edema.

Breast: The tissue was that of nonlactating breast. The stroma presented extramedullary hematopoiesis.

Skeletal Muscles: The normal architecture was distorted by severe edema.

Thymus: There was a decrease of thymocytes in the cortical lobules for a gland of this development, with marked infiltration of the stroma with erythroblastic islands.

*The general appearance and gross pathology are given only in such detail as to exclude the possibilities of fetal peritonitis, congenital elephantiasis, anomalies of the cardiovascular and biliary systems or of the thoracic duct, disomionphalo-angiopaghic monstrosities and other recognized causes of fetal dropsy.

Heart: There was hypertrophy of syncytial fibers with a relative increase of the nuclei.

Lungs: There was extensive infiltration of the parenchyma with erythroblastic islands. These were located principally in the sinusoids and periportal spaces, occasionally replacing the liver cells. The cell columns were compressed. Some of the cells showed early vacuolization. Iron stain was strongly positive.

Spleen: There was marked infiltration of red and white pulp by erythroblastic cells with derangement of the normal architecture. No Malphighian corpuscles were seen. Iron stain was positive.

Pancreas: Scattered islands of erythroblastic cells were present.

Adrenals: There were occasional islands of erythroblastic cells in the zona fasciculata.

Kidneys: There were scattered islands of erythroblastic cells in the cortex at the corticomedullary junction with numerous areas of these cells arranged in columns about the interlobular arteries. The tubules contained large deposits of yellow pigment. Parenchyma showed severe cloudy swelling. Iron stain was positive in the tubular area.

Ovary: There were several small blood-forming islands in the central hilum portion.

Bone: Sections of sternum, rib, femur, tibia and humerus showed marked hyperplasia of the marrow with predominance of the cells of the erythroblastic series. There was a lack of development of cortical bone despite the well-formed periosteum.

Brain: Normal tissue except for edema.

Placenta and Cords: The villi were larger than normal, blunt, and presented both a hyperplastic and an edematous stroma. The syncytial cells were large and vesicular with partial persistence of Langhan's layer. There were small islands of hematopoietic activity within the stroma of the hyperplastic villi. The capillaries contained many cells of the erythroblastic series. Wharton's jelly presented a loose edematous alveolar structure.

The body of Baby A was kept in fixing solution for twenty days before autopsy, but, despite this, generalized edema was still apparent, particularly in the eyelids and scalp. There were no gross developmental abnormalities. The abdomen was moderately distended. Inspection of the organs in situ revealed no abnormalities of lungs, liver, spleen, gastrointestinal tract, cardiovascular, biliary, or lymphatic systems or the pelvic organs. The heart and liver were grossly enlarged. A review of the sections showed extramedullary hematopoiesis in the thymus, spleen, pancreas, and kidney, with hyperplastic bone marrow. Iron stains were positive in the liver, spleen, and kidneys.

Taddei, Antonia: Vaginal Lesions From Potassium Permanganate, Rassegna d'ostet. e ginec. **49**: 61, 1940.

The author describes in detail 2 cases of patients with genital lesions produced by potassium permanganate introduced into the vagina as an abortifacient. He completely reviews the literature on this subject and summarizes in detail the characteristic pathology, symptomatology, differential diagnosis, clinical course, complications, and treatment of this condition.

CLAIR E. FOLSOME.

VAGINAL BLEEDING FROM POTASSIUM PERMANGANATE BURNS

JOHN C. SHULL, M.D., BOSTON, MASS.
(From the Boston City Hospital)

IN THE years 1936 through 1940 there have been admitted to the Gynecological Service of the Boston City Hospital 17 cases of vaginal bleeding secondary to vaginal or cervical burns from the insertion of potassium permanganate tablets. These cases present a uniform clinical picture which may be easily confused with a threatened or incomplete abortion. Inasmuch as there is no record of similar cases in the literature it has seemed worth while to report them.

Following is the record of a typical case:

Mrs. A. F. (No. 951768), aged 25 years, was admitted at 9 P.M. Sept. 20, 1939. She had had one full-term forceps delivery; she had undergone no operations and had no serious illnesses. Her periods were regular, the last period being June 19. She was admitted with the complaint of profuse vaginal bleeding, passing bright blood and clots. She had experienced no cramps and passed no tissue. She denied attempted induction. Examination revealed a pale nervous young woman in slight shock; blood pressure was 90/54, and pulse 100. General examination was otherwise negative. Pelvic examination showed a parous introitus. The cervix was closed, irregular, and firm. The uterus was that of a six weeks' pregnancy. There were two circumscribed charred areas about 2 cm. in diameter, one on the anterior vaginal wall anterior to and to the left of the cervix and one similar lesion on the posterior vaginal wall just posterior to the cervix. There was a general bloody ooze coming from the anterior lesion. A pack was inserted.

Direct questioning brought the admission that she had inserted a potassium permanganate tablet into the vagina the night before admission.

The hemoglobin was 60 per cent, red count 3.00 million, white count 13,200. The pack was removed in forty-eight hours. She ran a low grade febrile course and was discharged on the sixth hospital day to the prenatal clinic.

On April 14, 1940, A. F. was admitted to the Obstetrical Service in labor and delivered normally a living female, weighing 7 pounds 10 ounces. She had an uneventful convalescence and on the day of discharge a manual and speculum examination revealed no scar nor adhesion which might have resulted from the potassium permanganate burn.

This case exhibits the three characteristics common to all of the 17 cases, namely: painless profuse bleeding; tightly closed cervical os; and a circumscribed, charred vaginal lesion which could be visualized by speculum examination.

While 5 of the 17 women denied using the tablets to induce abortion, 15 had a period of amenorrhea of one day or longer. One of the remaining patients inserted the tablet on the day of the expected period, and the seventeenth patient had a positive Aschheim-Zondek test. It would seem, therefore, that in all the cases the tablet had been inserted to encourage a menstruation.

For treatment six of the patients required only bed rest. Nine were packed for twenty-four to forty-eight hours to stop the bleeding. In two cases the burn had eroded a small artery which required suture. The average hospital stay was five and one-half days.

It was possible to get a follow-up report of 10 of the 17 patients by a search of the out-patient records and by examination of the 6 patients who came to the hospital in response to invitations. Only one patient miscarried two days after discharge from the hospital. Five were not pregnant. Three delivered at term. Two others had positive Aschheim-Zondek tests. Only one patient of 10 had a vaginal-vault adhesion that seemed secondary to the chemical burn.

The patients were of different religious affiliations and of various nationalities. All were white. Their ages ranged from 19 to 36 years. There were no cases in the records of the Boston City Hospital previous to 1936.

SUMMARY AND CONCLUSIONS

There have been 17 cases of vaginal burns from the insertion of potassium permanganate tablets admitted to the Boston City Hospital since 1936. The tablets in all cases were inserted to simulate or stimulate menstruation. Diagnostic points were painless vaginal bleeding following a period of amenorrhea, a tightly closed cervix, and one or two circumscribed charred lesions in the vagina 1 to 3 cm. in diameter. Only one patient miscarried, and she after discharge from the hospital. No connection between the cases could be found.

These cases are readily confused with threatened and incomplete abortion. They emphasize the importance of manual and speculum examination of patients with threatened miscarriages.

A PORTABLE OBSTETRIC DELIVERY TABLE

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(From the Department of Obstetrics and Gynecology, Washington University)

THE importance of proper position of the patient in home obstetrics is emphasized in the publication *Maternal Care Complication,* edited by Dr. Fred L. Adair, approved by the American Committee on Maternal Welfare, Inc. Quoting from page 88, "The day has gone when those doing obstetrics should be satisfied with the makeshift arrangements accorded them in the past. The patient should be on a table of suitable height and should be properly supported by assistants or mechanical leg holders. She should be properly anesthetized, draped, and in a good light."

Anyone with experience in home obstetrics knows the unreliability of "family assistants" as leg holders, the lack of a suitable table to support the patient and the unsatisfactory results of relying upon the average household to have mechanical equipment suitable for an obstetric delivery. It would be reasonable for a patient to expect that the furnishing of such necessary equipment would be the responsibility of the physician, just as any tradesman is expected to furnish the equipment and tools necessary for his work.

Several years ago, after being unable to find suitable equipment for the securing and maintenance of proper position of the home obstetric patient, the idea was suggested of constructing a portable obstetric table. The problem was more complicated than was anticipated, and we have learned many reasons why suitable equipment had not been developed. Various mechanical devices, clamps, brackets, part tables, full tables, all with numerous modifications were given trial to procure a sturdy, compact, lightweight, portable and economical unit which would assist the physician in providing and maintaining proper position for the "home" obstetric patient.

The unit developed is a table* as illustrated, weight 35 pounds, easily portable, carried in a canvas case. It is fabricated from aluminum and cold rolled steel with chromium plate. The table legs and all working parts can be folded into the hollow interior of the table top in which the Bierhoff leg crutches and hand restraint cuffs are also transported. The table, set up, is sturdy, 21¼ inches wide, 50½ inches long, 36½ inches high. It provides adjustable Bierhoff leg crutches with canvas restraints and canvas hand restraint cuffs. The table can be set up in a few minutes.

This type of table has been used extensively at Washington University, St. Louis, Mo., and the Orange County Maternity Service, Santa Ana, California, and has given satisfactory service.

*The table is manufactured by A. S. Aloe Co., 1819 Olive St., St. Louis, Mo.

Fig. 1.

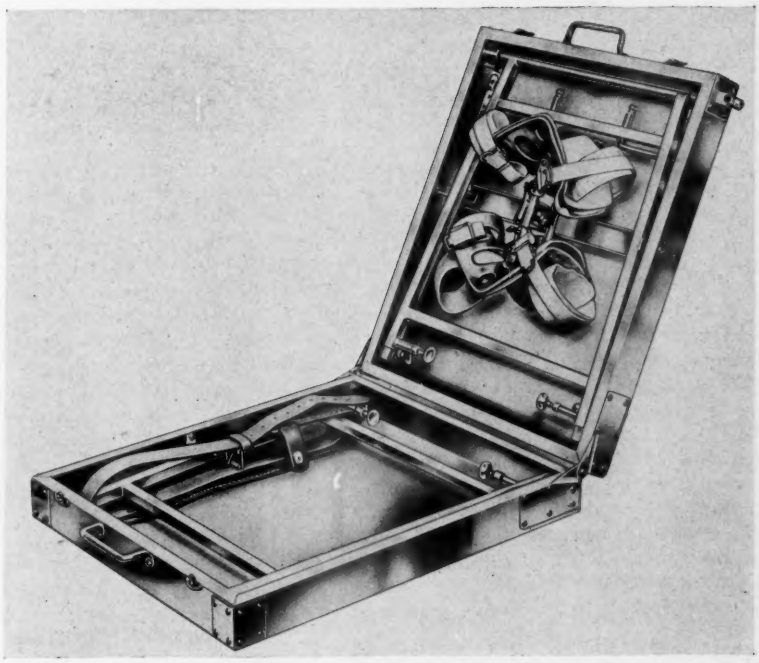

Fig. 2.

This table will provide:

1. Proper position for normal delivery.
2. Proper position for episiotomy, version, breech and forceps delivery, and other obstetrical operations.
3. A portable unit for obstetric and gynecologic clinics.

It is not recommended that this table should be used for every home obstetric patient, because there are factors of lack of time, assistants, et cetera which must be considered. However, in many instances these obstacles and disadvantages are not present or can be eliminated by foresight. Even in hospital obstetric practice, emergencies occasionally arise wherein it would be inadvisable and dangerous to insist that without exception, every patient had to be placed on the obstetric delivery table for delivery.

SUMMARY

1. Proper position of the patient is necessary for efficient obstetric care.
2. The practice of obstetrics in the home has been handicapped by the lack of facilities to provide and maintain proper position of the patient during delivery and other obstetric operations.
3. The standards of Class A hospital obstetrics could not be maintained without suitable mechanical equipment.
4. Portable mechanical equipment to provide proper position of the patient can be a valuable aid in eliminating some of the handicaps in home obstetrics, and promote new concepts of safety, comfort, and refinement in the care of the "home" obstetric patient.

Buhmann, Af Arne: The Treatment of Gonorrhea with Sulfapyridine, Ugesk. f. laeger **40**: 1159, 1939.

Of 90 cases of gonorrhea treated with sulfapyridine, 26 were in women and 4 in female children. Eleven of the women had received previous treatment with one or two series of sulfanilamide and two of the children had received previous treatment, one with sulfanilamide, the other with estrogen, sulfanilamide, and local applications.

The dosage for the women was 21 Gm. in seven days given in the following manner: 0.5 Gm. 8 times for two days, 0.5 Gm. 6 times for three days, and 0.5 Gm. 4 times for two days. Smears became negative to gonococci in from two to seven days following the beginning of the treatment, except in 2 cases in which the positive smear persisted for eleven and sixteen days, respectively. Twenty-five of the patients were considered cured after a period of observation which averaged eight weeks, but which ranged from two to seventeen weeks and during which an average of 8 negative smears were obtained. The one patient in whom there was a recurrence had received 16.5 Gm. of sulfapyridine in six days and had had a negative smear on the seventh day. On the fourteenth day, a positive smear was obtained and the patient was then lost from observation.

Toxic symptoms noted were headache, vertigo, nausea, vomiting, exanthemas, diarrhea, cyanosis, facial edema, icterus, and acroparesthesia. Only 11 of the 26 patients were free from toxic symptoms during the treatment. Headache, vertigo, and vomiting were the most common of the toxic effects and with the exception of one case of icterus which persisted for three weeks were relatively transient.

The children received a dosage of sulfapyridine which varied from 1/14 to 1/20 Gm. per kilogram of weight a day for from two to seven days. Only one patient had a toxic symptom which was vomiting. Two patients were cured and 2 were not.

CLAUDE J. EHRENBERG.

THE GYNEPAD, A RUBBER DIAPHRAGM TO BE USED IN PLACE OF LAPAROTOMY PADS IN PELVIC SURGERY*

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SURGEONS concede that the use of rough cloth pads in pelvic surgery produces considerable peritoneal trauma, with its consequences. Many modified pads have been devised in an attempt to avoid some or all of the inherent disadvantages. Most of these modified pads take the form of a rubberized bag or envelop in which may be inserted a towel or pad to lend body to an otherwise flaccid covering. While all of these combinations have several advantages, most of them still have some of the undesirable features of the cloth pads. For example, it is usually necessary

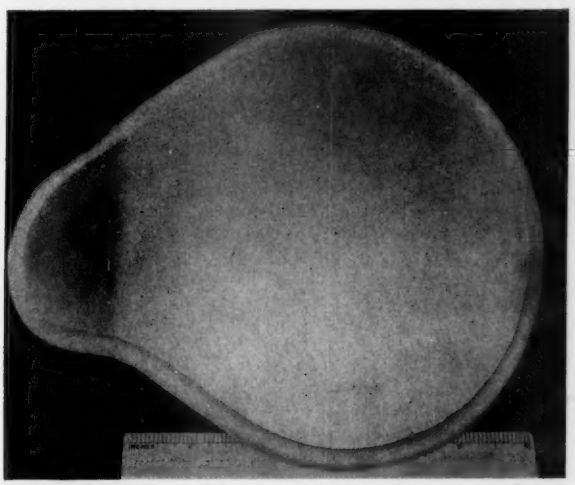

Fig. 1.—Top view of gynepad.

to use two or more of them in the average pelvis, thereby offering more opportunity for prolapse of intestine into the operative field. Also, they form a bulky mass which is difficult to retain in place, and offers little protection against upper abdominal contamination from the pelvis.

The "gynepad" has been designed to overcome these difficulties. It is a molded gum latex rubber diaphragm approximately six inches in diameter (Fig. 1) with a smaller tongue-like projection which is shaped to fit well into the pelvic culdesac. This small projection forms an angle of approximately 130 degrees with the larger surface of the diaphragm, in order to compensate for the promontory of the sacrum. All surfaces are smooth to eliminate trauma. Sufficient rigidity is obtained by having a molded bead about the periphery.

Satisfactory introduction and placement of the "gynepad" may be accomplished in any one of a number of ways. When one is operating through a midline incision, it is easily introduced after being folded longitudinally into three thicknesses (Fig. 2). The upper angle of the incision is lifted with a retractor and the corresponding end of the "gynepad" is introduced into the peritoneal cavity sufficiently to allow the tongue-shaped end of the pad to be placed in the culdesac. The pad is then released and allowed to spread itself over the intestinal mass. When operating

*Presented at a meeting of the New York Obstetrical Society, May 14, 1940.

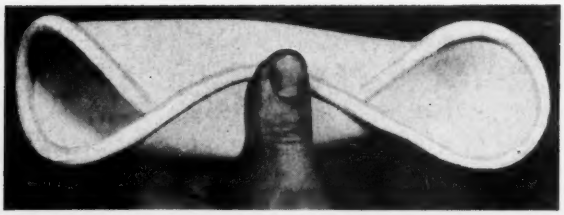

Fig. 2.—Method of holding gynepad when it is to be introduced through a midline incision.

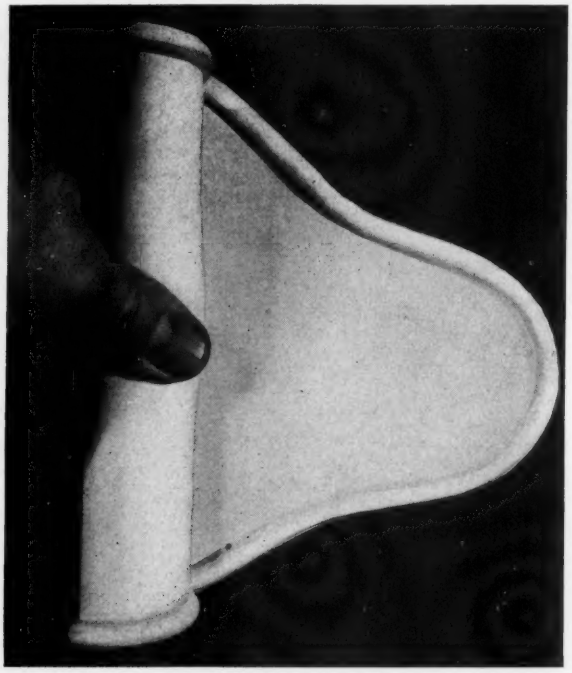

Fig. 3.—Method of rolling gynepad when it is to be introduced through a Pfannenstiel incision.

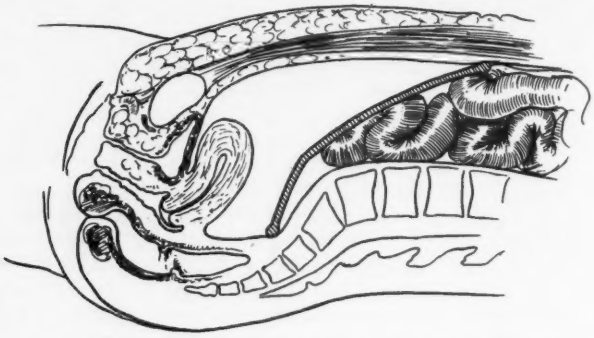

Fig. 4.—Lateral view of gynepad in position.

through a Pfannenstiel incision, it may be found advantageous to roll the pad from top to bottom (Fig. 3), introducing first one side and then the other into the peritoneal cavity. The technique of introduction, however, will undoubtedly be modified by each operator to suit himself.

The "gynepad" seems to work best when the patient is maintained in a very slight Trendelenburg position. Since intestinal pressure maintains the pad in close apposition with the lateral and anterior peritoneum, it is not necessary to have the patient in a profound state of anesthesia in order to have a clear operative field. If, for any reason, such as teaching, one prefers an exaggerated Trendelenburg position, then the "gynepad" may be maintained in the pelvis by passing a silk suture through its upper part and fastening this suture to the fascia at the upper angle of the incision.

When properly placed, the "gynepad" divides the peritoneal cavity into two parts (Fig. 4), the upper containing the intestines, and the lower, which is left free for any desired surgical procedure.

Briefly, then, the "gynepad" is a flexible gum rubber pad designed to keep the pelvis free of intestine during a laparotomy. It is incapable of producing peritoneal trauma, is easily introduced and removed, can be repeatedly sterilized by boiling, may be used for long periods of time, and acts as a tight-fitting barrier between the operative field and the remainder of the peritoneal cavity. It is economical, easy to use, and should save considerable time in most pelvic laparotomies.

The "gynepad" may be obtained from The Alco Rubber Company, 1945 Park Avenue, New York, N. Y.

Society Transactions

NEW YORK OBSTETRICAL SOCIETY

Meeting of May 14, 1940

The following case report and papers were presented:

Maternal Death Caused by Hemorrhage in the Adrenals. Dr. R. A. MacKenzie. (For original article, see page 150.)

The Gynepad, a Rubber Diaphragm to Be Used in Place of Laparotomy Pads in Pelvic Surgery. Dr. J. R. Gepfert. (For original article, see page 165.)

An Historical Review of Placenta Previa. Dr. James P. Marr.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D.

Selected Abstracts

The Puerperium

Benedik, A.: The Lochia, Monatschr. f. Geburtsh. u. Gynäk. **107:** 73, 1938.

One thousand puerperal women were studied to determine the quality and quantity of their lochial discharge. Blood-red lochia often persist longer than eight to ten days. This increased duration of red lochia is not always a sign of any pathologic disturbance. The author maintains that we cannot come to any decisions concerning the degree of involution of the uterus from the color of the lochia alone. If no other contraindications exist, women with red lochia may be permitted out of bed and may be allowed to leave the hospital. The author found that red lochia persist longer in elderly primiparas and in women who do not nurse their babies. Other factors in the determination of the color of the lochia are hypoplasia, frequently repeated pregnancies, persistent fever during the puerperium, prolonged labor and operative deliveries. Elevation of blood pressure is important in determining the color of the lochia only in the cases of pregnancy toxemias. Ergot preparations produce a more rapid disappearance of red lochia.

J. P. GREENHILL

Phillips, Miles H.: The History of the Prevention of Puerperal Fever, Brit. M. J. 1: 1, 1938.

The author gives a very comprehensive survey of the history of puerperal sepsis and a review of prophylactic measures, dating from about the middle of the nineteenth century.

The fundamental principle of contagion was suggested by Alexander Hamilton in 1781, demonstrated by Alexander Gordon in 1795, and supported vigorously by Oliver Wendell Holmes in 1843. The author shows that outbreaks of puerperal sepsis in hospitals and localized communities gave impetus to investigative efforts. These have occurred over the entire world.

Leeuwenhoek's discovery of micro-organisms with his primitive microscope, Pasteur's proof that micro-organisms cause disease, and Lister's application of these findings to his aseptic and antiseptic technique are examples of discoveries that have revolutionized surgical technique. Semmelweiss in Vienna deserves unlimited credit for his observation of the mode of spread of the dreaded infection from one patient to another.

The discovery of transmission by fomites and subsequent use of masks to prevent transmission of germs from the noses and throats of attendants was another step forward in the war against this disease. Credit for this must go to Hübener, Flügge, Mikulicz, and others. Surgeons were quicker to accept these new discoveries than were obstetricians. The author states that the pioneer in the use of the mask in obstetric practice is Joseph B. DeLee. Scientific support for the theory of air-borne infections from respiratory tracts of attendants finally came, resulting in general acceptance of the use of the mask but only after DeLee had been advocating it for no less than twenty years.

Special recognition is given to the work of Colebrook. Mention is also made of J. Whitridge Williams' calling attention to the possibility of parturient women conveying the organisms on their fingers to the vulva and vagina.

After a review of modern air conditioning and treatment of air with ultraviolet light, the author concludes with the statement that the most complete surgical technique is essential in really safe obstetric practice.

F. L. ADAIR AND JOHN A. HAUGEN

Theron, R.: Puerperal Sepsis at Home and in Hospital, South African M. J. 12: 9, 1938.

Since in England, as well as in many other countries, there has been no decrease in the death rate from puerperal sepsis during the last twenty years, the author had decided to review the situation and to make comparisons between home and hospital deliveries. A history of our knowledge of puerperal sepsis and its etiology is given. Semmelweiss' epochal discovery in 1847, with Pasteur's and Lister's discoveries later, marks the beginning of modern concepts of the disease.

The author states that the present death rate from puerperal sepsis in England is 1.7 per 1,000 live births, as compared with 1.42 twenty years ago. The apparent retrogression rather than improvement may be due to a changing basis for death certification and also changes in the classification for statistical purposes. However, the advances in the antenatal care and in general welfare work of recent times make the comparative results all the more disappointing.

A review of the bacteriology is given. The list of causative agents includes streptococci (hemolytic and nonhemolytic) (aerobic and anaerobic), *S. viridans, Staphylococcus aureus* and *albus,* pneumococcus, gonococcus, *Bacillus welchii,* and others. He lists all abnormalities of labor which cause prolongation of labor, excessive trauma to the soft tissues, hemorrhages, and instrumental deliveries (except simple low forceps operations conducted in ideal surroundings) as predisposing causes of infection. Eighty to ninety per cent of all cases are due to some type of streptococcus. Also he adds that the nonhemolytic strain can be found in the vaginas of nearly all women before labor, but the hemolytic variety can rarely be found in healthy women and is commonly found in infected cases, both in the uterus and in the blood. Anaerobic streptococci can be found in the genital tract of pregnant women and women in labor and rank second only to the hemolytic streptococcus as a causative agent in puerperal infection.

The author theorizes that the hemolytic streptococci are probably always conveyed to the genital tract extrinsically, either by droplet or by the hand or instrument of an attendant. Also the curve of incidence of puerperal morbidity follows fairly closely the seasonal curve of incidence of influenza and colds.

Resistance of the patient and also vitamin deficiency are discussed in connection with the etiology.

The discussion of treatment is dismissed with a few words on general supportive measures. Prevention implies ensuring the health of our expectant mothers plus early recognition of conditions of a mechanical nature, such as contracted pelves.

A rigid technique as regards asepsis will do much to lower the present morbidity. Antiseptics too are steadily being improved. The author reviews Colebrook's work on the efficiency of various antiseptics.

In conclusion, he summarizes that comparative figures for home and hospital practice are unfair, because the complicated cases are always moved to a hospital and the simple cases are left in the home. Home delivery services should be under the supervision of institutions. Institutions should guard against unnecessary interference with normal cases, adhere to strict isolation of infected cases, and have rigid rules for technique in asepsis and antisepsis. The result should be a lowering of morbidity and mortality rates.

F. L. ADAIR AND JOHN A. HAUGEN

Fleming, Amy M.: Puerperal Sepsis and Haemolytic Streptococci, Brit. M. J. 2: 639, 1939.

It was estimated that not less than 85 per cent of fatal infections following normal deliveries in England in 1932 were due to hemolytic streptococci. Lancefield and Hare later showed that almost all the infecting strains in severe puerperal sepsis belonged to Group A hemolytic streptococci.

Throat swabs taken on 120 medical students prior to work on the maternity wards showed 22.5 per cent had hemolytic streptococci and 4.2 per cent (five students) had the Lancefield Group A strain. Four of these 5 at the time were working on the children's ward. No relationship was noted between the incidence of Group A strain and the presence of tonsillar tissue.

Treatment consisted of moderate outdoor exercise, swabbing, and administration of prontosil. Persistence of positive throat swabs was noticeable in those whose nasopharynx was in an unsatisfactory condition.

FRED L. ADAIR AND J. R. KIGHT.

Cosgrove, S. A., and Barry, Thomas A.: Antepartum Gas-Bacillus Infection, New England J. Med. 222: 344, 1940.

The authors describe a case of ante-partum infection with *Clostridium welchii* leading to infection of the fetus by way of placenta and resulting in a stillbirth. Under serum treatment supplemented by sulfanilamide the patient had an uneventful post-partum course except for an afternoon temperature rise up to 101° F.

From study of the literature the writers conclude that the *Clostridium welchii* will not by itself cause damage unless the conditions are suitable. As the liberated toxins devitalize more tissue the infection progresses. The uterus is a perfect incubator and the dead fetus an excellent medium for growth. Since there is no way of telling that the dead fetus is infected, one is forced to await the outcome of delivery before making a diagnosis. Surgery has no definite place in the therapy, forcing the obstetrician to be conservative. Sulfanilamide seems of value.

HUGO EHRENFEST

Delmas, P., and de Kereau, J. C.: Attempts at Prophylaxis of Puerperal Infection by Means of Sulfamides, Bull. Soc. d'obst. et de gynéc. 27: 711, 1938.

A series of 493 puerperal women were given sulfanilamide as soon after delivery as possible and for at least four days afterwards. The authors observed that following this prophylactic therapy there was a slight decrease in mortality and a considerable reduction in morbidity. The reductions were sufficient to justify continued use of this prophylactic medication.

J. P. GREENHILL

Schäfer, Gunther: A Study of the Bactericidal Power of the Blood After Chemotherapeutic Prophylaxis During Pregnancy and Puerperium, Deutsche med. Wchnschr. 66: 240, 1940.

Using cultures of hemolytic streptococcus, Schäfer was able to do 187 tests on the blood of 125 women who were divided into three groups: untreated, taurolin-treated and prontosil-treated. Blood samples, taken at various intervals during pregnancy and the puerperium, were inoculated with fresh cultures in a dilution of 1/10,000 and incubated for three to six hours, then poured on sterile plates. The criterion of the effect on virulence was taken from the effect on the appearance and count of colonies.

In untreated cases a diminution of bacterial virulence was found in the first and second halves of pregnancy. During the event of labor, virulence increases, remaining at a high point until the fifth to seventh day post partum, when a temporary increase in natural bactericidal power was shown. From the seventh day the virulence was shown to be increased. The taurolin- and prontosil-treated cases showed a definite increase in bactericidal power during pregnancy, labor, and puerperium. In operative deliveries no significant variation in effect on bactericidal power was noted. The author attempts to provide a bacteriologic guidepost for chemotherapy in pregnancy. Dosages of taurolin and prontosil are not given.

R. J. WEISSMAN

Baird, D., Michie, A., and MacDonald, R.: Prevention and Treatment of Puerperal Sepsis, Lancet 2: 148, 1939.

After a study of puerperal sepsis in the city and county of Aberdeen, Scotland, the authors feel that the following conclusions are justified. In a well-run maternity unit, where strict control of all contacts during labor and the puerperium is obtainable, the incidence of streptococcal sepsis can be reduced to a very low level. This incidence depends on the presence of the organism in the genital tract during labor, the patients' resistance, and the amount of trauma sustained. Most of the deaths from such sepsis are caused by the hemolytic streptococcus Group A, absent from the genital tract before labor. The access of the organism to the genital tract can be prevented by asepsis, antisepsis, the use of masks, and the exclusion of carriers of streptococci from the labor room. The risk of infection is much less when the entire labor is conducted in the hospital.

The maternal deaths in Aberdeen are analyzed in two periods: 1931 to 1935 and 1936 to 1938 which are before and after the introduction of sulfanilamide therapy. There was a fall in death rate from 6.2 to 4.6 per thousand due mainly to a fall in the death rate from sepsis from 2.05 to 1.02 per thousand. An analysis of the cases of puerperal sepsis during these two periods shows a fall in the total case mortality from 13.9 to 9.0 per cent and a fall from 19.2 to 8.3 per cent in the case mortality of sepsis due to the hemolytic streptococcus.

It was found that with easy delivery the case mortality in puerperal infection was 12.7 per cent before the introduction of sulfanilamide therapy and 4.1 per cent after. With difficult delivery, the mortality was 28.9 per cent before and 12.8 per cent after sulfanilamide introduction. In spite of sulfanilamide therapy, therefore, the prognosis is poor in hemolytic streptococcal infection in the presence of extensive local trauma.

CARL P. HUBER

Gordon, Charles A., and Rosenthal, Alexander H.: Sulfanilamide Therapy in Severe Puerperal Infection, Surg. Gynec. Obst. 69: 631, 1939.

Large doses of sulfanilamide were given to 118 patients with severe puerperal infections of the genital tract, regardless of their etiology. Clinical response was prompt and satisfactory in 45 cases, or 38 per cent. In an additional 45 cases, or 38 per cent, results were not convincing, yet good enough to deduce that the drug may have played an important part in recovery. In 23 cases, or 20 per cent, no beneficial results were observed. There were 5 deaths, a mortality of 4 per cent.

Administration is definitely associated with toxic manifestations, none of which need be a serious hazard. Usually obvious and rarely severe enough to warrant discontinuance of therapy, toxicity is actually low. A moderate fall in hemoglobin is common and harmless. No case of agranulocytosis was seen. Acute hemolytic anemia cannot be foreseen or prevented since it is apparently due to idiosyncrasy, developing quickly within the first few days of treatment after comparatively small doses of the drug. Rapid drop in hemoglobin and erythrocytes, leucocytosis, marked reticulocytosis, bilirubinemia, and urobilinuria are noted. Daily blood counts for at least the first five days are essential. Though it occurs but seldom, and transfusion is effective, it is because of the ever present danger of serious blood changes that indiscriminate administration of sulfanilamide is inadvisable.

In mild cases of puerperal infection, sulfanilamide is not indicated. Certainly proper bacteriologic investigation should precede therapy, but it is not essential. Intrapartum infections should be treated with sulfanilamide at once. Report on *Streptococcus hemolyticus* may be had in twenty-four hours; vaginal swab culture is better than intrauterine. If hemolytic streptococci are found, drug therapy should be discontinued only under exceptional circumstances, and one should not be too quick to stop its administration because bacteria have disappeared or a diagnosis of drug fever has been made.

The most recent experience indicates that optimum benefit may be expected with spaced maintenance doses of 20 to 30 gr. of sulfanilamide and moderate fluid restriction, provided a large initial dose has been given the patient.

In severe puerperal infections of the genital tract whatever their etiology, sulfanilamide may be used and should be, provided the patient is in a hospital where its administration may be controlled.

WILLIAM C. HENSKE.

Bonafos: The Treatment of Puerperal Infection With Sulfamide Derivatives, Bull. Soc. d'obst. et gynéc. **28**: 344, 1939.

The author reports a series of 60 cases of puerperal infection treated with sulfamide derivatives. He believes that these drugs will play a very important role in the battle against these infections not only as a prophylactic but also as a curative measure. For the purpose of overcoming an already existing infection, the drugs must be given judiciously, early, and when there are not localized or diffuse suppurations which require surgical interference. Care, however, must be exercised in the use of these drugs. Necessary precautions are: avoidance of sulfates, absolute rest in bed, and the use of sodium bicarbonate.

J. P. GREENHILL.

Gayus, Greene-Armytage, and Baker: Puerperal Agranulocytosis Following Sulphanilamide Treatment, Brit. M. J. **2**: 560, 1939.

A fatal case of puerperal agranulocytosis following sulfanilamide therapy is reported. It clearly demonstrates the value of frequent blood studies, and points to the possibility of a serious and perhaps fatal upset of the hematopoietic system from sulfanilamide therapy.

FRED L. ADAIR AND JOHN R. KIGHT.

Keller, R., and Limpach, J.: Blood Transfusion in Generalized Puerperal Infection, Rev. franç. de gynéc. et d'obst. **34**: 129, 1939.

In the opinion of the authors blood transfusion has a favorable effect in cases of generalized puerperal infection. This is manifested by a sudden fall in temperature and pulse rate, by a suppression of chills and by improvement in the general condition. The earlier the transfusion is given the better the result. To obtain the best results the blood must be given as soon as the infection becomes generalized. Furthermore, the transfusions must be repeated at five- to eight-day intervals. They are useless when given late, particularly if there are metastases and serious septic lesions in important organs.

Contraindications to the use of blood transfusions are endocarditis, nephritis, hepatitis, and acute pulmonary infections. Generally only between 150 and 200 c.c. of blood should be given at one time. The authors used citrated blood, unmixed blood, and placental blood, and they observed no apparent differences.

The authors believe that there is no doubt about the great value of blood transfusions and that this therapy is the best we possess today to combat generalized puerperal infection.

J. P. GREENHILL.

Ramos, Alberto P., and Montes, Alberto A.: Slow Hyper-Arseno-Transfusion (Drop by Drop), as Treatment of Grave Puerperal Infection, Presse méd. **48**: 530, 1940.

The authors modified Tzanch's "Massive Arsenotherapy" treatment described for use in seriously ill puerperal sepsis cases. Other authors have utilized serum, physiologic saline, or glucose solutions as diluents for administration of an arsenical in massive arsenotherapy. Ramos and Montes administer the arsenical in the vehicle of a small transfusion of weakly citrated blood. The authors designate their treatment as "slow hyper-arseno-transfusion." This phrase clearly implies the therapeutic action they wish to accomplish.

The technique used is described as follows: 150 cg. of neosalvarsan, diluted in 3 or 4 c.c. of glucose solution, is added to 200 c.c. of weakly citrated (20 c.c. of 2 per cent citrate solution) blood. The hyper-arseno-transfusion fluid is placed

in a transfusion bottle, elevated 160 cm. and allowed to *drip slowly* into the vein during the next three to three and one-half hours. The rate of flow is about 20 drops a minute. It is wise to avoid chilling of the blood.

To protect the hepatic function the authors inject at the end of the transfusion, via the same intravenous needle, 50 to 80 c.c. of hypertonic glucose. Immediately after the intravenous hypertonic glucose, 10 cg. of vitamin C and whole liver extract are given intramuscularly. Cardiazol, epinephrine, etc., are used as necessary preliminary medications.

Six abstracted cases are presented, five of these illustrated by reduced graphic sheets. The one fatal outcome was due to an infectious endocarditis; it was the only one of the 6 cases with a positive blood culture.

The reactions to the treatment were adjudged not to be severe. One patient collapsed upon initiation of the treatment but was quickly aroused with stimulants. Transitory anuria was treated in one case. Mild icterus and bronzing (characteristic of saturation) and mild diarrhea were the only other reactionary symptoms.

The authors gave a total of 2 ''slow hyper-arseno-transfusions'' one a day for two days, to each of three patients. The temperature and pulse in most instances rapidly fell to normal They note that it has never been necessary to give a third ''slow hyper-arseno-transfusion,'' for beneficial results are obtained after the first or immediately after the second transfusion.

CLAIR E. FOLSOME.

Barr, John B.: The Remote Effects of Puerperal Sepsis, Brit. M. J. 1: 1132, 1939.

In an attempt to determine the remote effects, the author examined 200 patients who had had puerperal sepsis four to six years previously. The examination consisted of the patient's medical and obstetric history before and after the puerperal illness, a general medical, and pelvic examination, including bacteriologic study of the upper vaginal secretion, and a radiologic examination when necessary.

The author found sterility in 77 patients (38.5 per cent), although in 33 (16.5 per cent) this condition may have been due to the use of contraceptives. A noteworthy feature was the increased tendency of abortion, the abortion to labor ratio being 1 to 5.7 before sepsis and 1 to 2.8 afterwards. Also there was an incidence of subsequent sepsis, being 58 per thousand in the patients with sepsis (corrected by author to 39 per 1,000) as compared to 25.1 in an unselected group. As to the general health, a thing difficult to assess was the fact that only 38 per cent had suffered in any way severely.

Gynecologic examinations revealed lesions in 78 per cent of the patients. A total of 237 lesions were found of which chronic cervicitis constituted 57 per cent, chronic corporeal infection 24.4 per cent, chronic pelvic cellulitis 60 per cent, and chronic salpingo-oophoritis 12.6 per cent. Extragenital lesions included persistent phlegmasia in 21 cases.

In the majority of the patients the original organism was the *Strep. hemolyticus,* but in no instance did the present bacteriologic study demonstrate this organism in the vagina.

FRED L. ADAIR AND JOHN NEWDORP.

Harer, W. Benson, and Sharkey, John A.: Acute Inversion of the Puerperal Uterus, J. A. M. A. 114: 2289, 1940.

The authors report one instance of acute inversion of the puerperal uterus seen in 16,240 obstetric cases. They review the chief causes of inversion of the uterus. Suprafundal pressure is mentioned as the most frequent cause of the acute inversion. Mention is made of the causal factors in spontaneous inversion of the uterus, such as increased intra-abdominal pressure brought about by sneezing, coughing, and vomiting. Another theory has been advanced that there is abnormal distribution of the muscle fibers of the fundal portion of the uterus with a preponderance of the circular fibers over the longitudinal ones in some of these

cases. In certain other cases there seems to be some abnormality in the innervation of the uterus which results in abnormal contraction of the uterine muscle fibers and the production of inert areas or softening of the uterine wall. Mortality in these cases is high (40 per cent, Cooke). Hemorrhage and shock remain the most important clinical signs. It is to be differentiated chiefly from a prolapsed submucous fibroid. Treatment varies from immediate replacement of the inverted uterus to deferring replacement until after recovery from the shock. The authors advise replacement by gentle taxis associated with active antishock treatment. The cervix may be relaxed by injection of adrenalin (1:1000). In a total of 13 patients treated this way, the authors had 11 recoveries and 2 deaths. Where the cervix is tightly constricted, either the Küstner or Spinelli operation is indicated. Cesarean section is indicated in subsequent pregnancies if inversion had been treated by a surgical procedure.

WILLIAM BERMAN.

Correspondence

Contraceptive Practice

To the Editor:

Having read with keen interest your thoughtful paper, "Contraceptive Practices," in the Anniversary Number (October, 1940) of the AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, we wish to thank you for it, and at the same time to draw your attention and that of your readers to some wrong impressions which certain of its passages may tend to create.

On page 653, in speaking of "the so-called 'clinics'"—(correctly so termed)—"which are accessible to the general public," you state that it is in these "that reform is necessary." Your reason appears to be that, because many of these centers are not connected with established hospitals, they "are operating usually without the pale of the law . . . . and, therefore, uncontrolled by any supervising authority except the local policeman." Clinics approved by the Birth Control Federation of America are operated in full accordance with authentic interpretations of state and federal law.

A recent report on birth control centers in the United States* points out that at the close of 1939, 549 centers were functioning *under medical direction* in 42 states. This direction is by licensed physicians such as those serving in hospital clinics, in many cases the same physicians. They are members in good standing of their medical societies. Such centers cannot, therefore, be described as "uncontrolled by any supervising authority except the local policeman," unless the physicians in charge may be said to function as policemen.

We wholly concur in your hope that in the near future all hospitals will install contraceptive clinics, following such leads as that of Albany Hospital and Strong Memorial in New York State, of Johns Hopkins in Baltimore, The University of California Hospital, San Francisco, and about one hundred others. We need not re-emphasize to you the difficulties and opposition which must be overcome before this goal is reached. Should not effort to achieve it be part of the work of the liberal, civic-minded obstetrician, who is concerned not only with the management of pregnancy, but also with the occurrence of it under favorable, and not under unfavorable, conditions?

The fact that such clinics are needed for those whom you designate as the "medically indigent"—persons who tend to become civically indigent by lack of advice to protect against undesired or contra-indicated overproductiveness of children—is indicated in the above-mentioned Journal of the American Medical Association report. This showed that 34 per cent of new patients in a total of 46,582 were on relief or unemployed, and 60.5 per cent of the total were advised and given materials either without charge or for a fee of one dollar or less.

*Dickinson, R. L. and Morris, W. E.: Birth Control Centers: Report of 202 in U. S. for the year 1939, J. A. M. A. **115**: 591, 1940.

In your article, you infer on page 654 that if public health departments include contraceptive service, such activities are in conflict with "established Federal Statutes." Again allow us to correct you. The Federal Statutes on contraception apply only to distribution and importation of books and materials by mail or common carrier. They have been interpreted in the case of U. S. vs. One Package, 86F 2nd 737 (C. C. A. 2nd 1936) in the words of the decision. "Not to prevent the importation, sale, or carriage by mail of things which might intelligently be employed by conscientious and competent physicians for the purpose of saving life or promoting the well-being of their patients."

You may recall that this case was not taken by the Government to the United States Supreme Court for review because the U. S. Attorney General accepted this decision as law. It is, in consequence, definitive. The Federal Law, therefore, has no bearing on activities of a state public health department in providing contraceptive service.

The state laws, where they are restrictive, constitute the only barrier; otherwise the right of the physician to prescribe contraceptives for the patient has been unchallenged. In two states, Connecticut and Massachusetts, state laws have been construed by the courts as prohibiting physicians from advising on contraception. These laws state respectively that the *use* of a contraceptive is illegal, and that *offer* or *issuance* of a contraceptive is illegal. Curiously, medically indicated abortion and sterilization are legal in both states!

Your article contains so much that is helpful, sound and constructive that we regret the inclusion in it of any statement which is not in harmony with facts. Knowing that you would not wish to create a false impression, we are sending these corrections, and trust that they will receive early publication and prominence comparable to that of your excellent article.

Richard N. Pierson, M.D.
Robert L. Dickinson, M.D.
Ira S. Wile, M.D.
Woodbridge E. Morris, M.D.

Representing the Birth Control Federation of America.

New York, December 28, 1940.

A Reply

The foregoing letter is answered herewith by the undersigned as an individual, not as an editor of the JOURNAL. What I have to say therefore has no official implications in so far as this publication is concerned.

To begin with, I do not feel that I have erred in stating that most of the extramural clinics, namely those not connected with established hospitals, which exist for the public dissemination of contraceptive information, are operated without the pale of the law. The question of their supplying a demand for such services, is not under consideration. However, to the best of my knowledge, these particular clinics, sponsored by the Birth Control Federation of America, are not licensed by any constituted authority and therefore are not subjected to official control, regulation, or inspection, such as is imposed upon established dispensaries.

I repeat that I do not refer to those contraceptive clinics which are part and parcel of a hospital service but to those of definitely extramural character in which little distinction is drawn, in most instances, between perhaps questionable social and definite medical indications. It is here, I believe, that abuses can and do arise, a fact to which many physicians can testify. Not only the indigent but many other women freely patronize these readily accessible facilities in response to a widespread propaganda backed apparently by unlimited funds. The *Journal of the American Medical Association*, quoted by the protestants, shows that only 34 per cent of the treated patients come definitely into the indigent group, that 60 per cent of the total were given advice and treatment without any, or for a nominal charge (i.e., they were considered indigent), which still leaves about 40 per cent who, as a matter of fact, should not have been accepted under the common dispensary laws.

Moreover the statement in the letter that "clinics approved by the Birth Control Federation of America are operated in full accordance with authentic interpretations of state and federal laws," is entirely meaningless. This organization is a self-constituted group of interested individuals; it operates without authority and largely by favor, and while its clinics may be served by medical personnel in good standing, my contention still holds that such activities are uncontrolled by any supervising governmental authority. If those official bodies entrusted with such authority have not acted to assert it, this is a matter not for me to discuss. Incidentally it would be of interest to know how many centers operate outside of the 549 under medical direction or how competent this medical direction may be.

It is admitted in the above letter that "state laws, where they are restrictive, constitute the only barrier" ostensibly, to the operation of the extramural clinics. This would seem to confirm the contention that they are conducted illegally, using the term in a broad sense. However, academic discussions are hopeless in so far as achieving progress in the solution of this troublesome problem is concerned. It is generally accepted that there are definite medical indications which call for methods to avoid conception; possibly these should be extended to include certain social and economic situations if important from the medical viewpoint. If so, why not legalize this activity, through the medium of professional organization?

I do not feel that I have created any false impressions in my article. Until the dissemination of contraceptive advice through clinical facilities can be placed on a basis acceptable to the profession as well as to legally constituted authorities, we must look for further objections to the present scheme. All public dispensary facilities, no matter what their particular field of activity, should operate on the same plane of official supervision and control, and to stress this aim I consider to be one of the main purposes of my article. If this is unattainable, a discussion of pertinent facts does not appear to be out of place. It is only by this means that the abuses which have developed may be adequately handled and eliminated.

George W. Kosmak, M.D.

New York, December 15, 1940.

Item

American Board of Obstetrics and Gynecology

The general oral and pathological examinations (Part II) for all candidates (Groups A and B) will be conducted by the entire Board, meeting at Cleveland, Ohio, from May 28 to June 2, 1941, immediately prior to the opening of the annual meeting of the American Medical Association.

Application for admission to Group A (Part II) examinations must be on file in the Secretary's Office not later than March 1, 1941.

Formal notice of the time and place of these examinations will be sent each candidate several weeks in advance of the examination dates.

Candidates for *reexamination* in Part II must make written application to the Secretary's Office before April 15, 1941.

The Board requests that all prospective candidates who plan to submit applications in the near future request and use the new application form which has this year been inaugurated by the Board. The Secretary will be glad to furnish these forms upon request, together with information regarding Board requirements. Address Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh (6), Pennsylvania.

ROSTER OF AMERICAN OBSTETRICAL AND GYNECOLOGICAL SOCIETIES*

(Appears in January, April, July, October)

American Gynecological Society. *President,* E. J. Litzenberg. *Secretary,* Richard W. TeLinde, 11 East Chase Street, Baltimore, Md. Next meeting, May 26 to 28, 1941, Broadmoor Hotel, Colorado Springs, Colo.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons. *President,* Frederick H. Falls, Chicago, Ill. *Secretary,* James R. Bloss, 418 11th Street, Huntington, W. Va. Annual meeting will be held at the Homestead, Hot Springs, Va., September 11 to 13, 1941.

Central Association of Obstetricians and Gynecologists. *President,* Thomas B. Sellers, New Orleans, La. *Secretary-Treasurer,* W. F. Mengert, Iowa City, Iowa. Next meeting, New Orleans, La., Fall of 1941.

South Atlantic Association of Obstetricians and Gynecologists. *President,* M. P. Rucker, Richmond, Va. *Secretary,* Robert A. Ross, Durham, N. C. Next meeting, February 7 and 8, 1941, Jacksonville, Fla.

A. M. A. Section on Obstetrics and Gynecology. *Chairman,* Norman F. Miller, Ann Arbor, Mich. *Secretary,* Philip F. Williams, 2206 Locust St., Philadelphia, Pa. Next meeting, June 2 to 6, 1941, Cleveland, Ohio.

New York Obstetrical Society. *President,* Thomas C. Peightal. *Secretary,* Ralph A. Hurd, 37 E. 64th Street, New York City. Second Tuesday, from October to May, Yale Club.

Obstetrical Society of Philadelphia. *President,* Roy W. Mohler. *Secretary,* John C. Hirst, 500 North 20th St., Philadelphia, Pa. First Thursday, from October to May.

Chicago Gynecological Society. *President,* Harold K. Gibson. *Secretary,* James A. Gough, 104 S. Michigan Ave., Chicago, Ill. Third Friday, from October to June, Hotel Knickerbocker.

Brooklyn Gynecological Society. *President,* George G. Cochran. *Secretary,* John J. Madden, 362 Washington, Ave., Brooklyn N. Y. First Friday, from October to May, Kings County Medical Society, 1313 Bedford Avenue, Brooklyn, N. Y.

Baltimore Obstetrical and Gynecological Society. *President,* Abraham Samuels, *Secretary-Treasurer,* Frank K. Morris, 11 East Chase St., Baltimore, Md. Meets quarterly at Maryland Chirurgical Faculty Building.

Cincinnati Obstetrical Society. *President,* E. W. Enz. *Secretary,* Edward Friedman, 19 West Seventh St., Cincinnati, O. Third Thursday of each month.

Louisville Obstetrical and Gynecological Society. *President,* Esther C. Wallner. *Secretary,* Samuel S. Gordon, 520 Heyburn Building, Louisville, Ky. Fourth Monday, from September to May, Brown Hotel.

Portland Society of Obstetrics and Gynecology. *President,* Howard Stearns. *Secretary,* William M. Wilson, 545 Medical Arts Bldg., Portland, Ore. Last Wednesday of each month.

Pittsburgh Obstetrical and Gynecological Society. *President,* S. A. Chalfant. *Secretary,* Joseph A. Hepp, 121 University Place, Pittsburgh, Pa. First Monday of October, December, February, April, and June.

Obstetrical Society of Boston. *President,* Raymond S. Titus. *Secretary,* Judson A. Smith, 262 Beacon St., Boston, Mass. Third Tuesday, October to March, Harvard Club.

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*Changes, omissions, and corrections should be addressed to the Editor of the JOURNAL.

New England Obstetrical and Gynecological Society. *President,* Frederick L. Good. *Secretary,* R. J. Heffernan, 475 Commonwealth Avenue, Boston, Mass. Meetings held in May and December.

Pacific Coast Obstetrical and Gynecological Society. *President,* John Vruwink. *President-Elect,* T. Floyd Bell. *Secretary-Treasurer,* William Benbow Thompson. Next meeting, Los Angeles, Calif., November 5 to 8, 1941.

Washington Gynecological Society. *President,* R. L. Sylvester. *Secretary,* W. R. Thomas, 1830 K. Street, N. W., Washington, D. C. Fourth Saturday, October to May.

New Orleans Obstetrical and Gynecological Society. *President,* E. L. Zander. *Secretary,* Eugene Countiss, 921 Canal St., New Orleans, La. Meetings held every other month.

St. Louis Gynecological Society. *President,* E. Lee Dorsett. *Secretary,* Joseph A. Hardy, Jr., 4952 Maryland Ave., St. Louis, Mo. Second Thursday, October, December, February, and April.

San Francisco Gynecological Society. *President,* T. Henshaw Kelly. *Secretary,* R. Glenn Craig, 490 Post Street, San Francisco, Calif. Regular meetings held second Friday in month, University Club, San Francisco, or Claremont Country Club, Oakland, Calif.

Texas Association of Obstetricians and Gynecologists. *President,* Roy Grogan. *Secretary,* J. McIver, 714 Medical Arts Building, Dallas, Texas. Next meeting, Galveston, Texas, September, 1941.

Michigan Society of Obstetricians and Gynecologists (formerly the Detroit Obstetrical and Gynecological Society). *President,* Russell W. Allen. *Secretary,* Harold C. Mack, 955 Fischer Bldg., Detroit, Mich. Meeting first Tuesday of each month from October to May (inclusive).

Obstetric Society of Syracuse Hospitals. *President,* Francis R. Irving. *Secretary,* Nathan N. Cohen, 713 East Genesee St., Syracuse, N. Y. Meets second Tuesday of September, November, January, March, and May.

Alabama Association of Obstetricians and Gynecologists. *President,* T. M. Boulware, Birmingham, Ala. *Secretary,* Eva F. Dodge, 519 Dexter Avenue, Montgomery, Ala. Next meeting, Mobile, Ala., April, 1941.

San Antonio Obstetric Society. *President,* I. T. Cutter. *Secretary,* S. Foster Moore, Jr., San Antonio, Texas. Meetings held first Tuesday of each month at Gunter Hotel.

Books Received

L. EMMETT HOLT. Pioneer of Children's Century. By R. L. Duffus and L. Emmett Holt, Jr. Foreword by Edwards A. Park, Professor of Pediatrics, Johns Hopkins University. Illustrated. 295 pages. D. Appleton-Century Company, New York, 1940.

MULTIPLE HUMAN BIRTHS. By Horatio Hackett Newman, Ph.D., Sc.D., Professor of Zoology, University of Chicago. Illustrated, 214 pages. Doubleday, Doran & Co., New York, 1940.

FOREIGN BODIES LEFT IN THE ABDOMEN. The Surgical Problems and Legal Problems. By Harry Sturgeon Crossen, M.D., School of Medicine, Washington University, and David Frederic Crossen, LL.B., School of Law, Washington University, St. Louis. With 212 illustrations, including 4 color plates, 762 pages. The C. V. Mosby Company, St. Louis, 1940.

DISEASES AFFECTING THE VULVA. By Elizabeth Hunt, M.D., Ch.B. (Liverp.), Honorary Physician to the Skin Department, South London Hospital for Women, etc. With 36 illustrations and 18 plates in color. The C. V. Mosby Company, St. Louis, 1940.